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Rearrangement in Dihydroresorcinol Derivatives. II.[1] Synthesis of 3-Alkoxy and Hydroxy-2-cyclohexen-1-one Oximes[2]

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The synthetic methods for 3-alkoxy- (IIa,b,c and IIIa,b,c) and hydroxy-2-cyclohexen-1-one oximes (IVa,c) were established. Treatment of dihydroresorcinol (Ia), dihydroorcinol (Ib), dimedone (Ic) and their derivatives with hydroxylamine hydrochloride in methanol, ethanol and water afforded good yields of IIa,b,c, IIIa,b,c and IVa,c. The reaction mechanisms and configurations of the oximes are also mentioned. Inaddition, our experiments revealed that the Gittel's assignment on the product obtained the bytreatment of dimedone (Ic) and $NH_2OH \cdot HCl$ in ethanol was erronous, that is, the product was not 3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one oxime (IVc)assigned by him, but 3-ethoxy-5,5-dimethyl-2-cyclohexen-1-one oxime (IIIc).

3-Alkoxy and hydroxy-2-cyclohexen-1-one oximes were required for the investigation of Beckmann rearrangement of dihydroresorcinol derivatives.[1] Gittel reported[4] that 3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one oxime was obtained by the treatment of dimedone with $NH_2OH \cdot HCl$ in ethanol. However, our experiments revealed that the assignment of the product was erronous, that is, the produced oxime was not the one assigned but 3-ethoxy-5,5-dimethy-2-cyclohexen-1-one oxime. Therefore, we have investigated the oximation of dihydroresorcinol (Ia), dihydroorcinol (Ib), dimedone (Ic) and their derivatives. As a result, it was established that reactions of 3-hydroxy-2-cyclohexen-1-ones (I) with $NH_2OH \cdot HCl$ in methanolic, ethanolic and aqueous solutions gave 3-methoxy (II), 3-ethoxy (III) and 3-hydroxy-2-cyclohexen-1-one oximes (IV), respectively, and the procedures were suitable for preparative purpose. The present paper describes the preparations of 3-alkoxy and hydroxy-2-cyclohexen-1-one oximes (IIa,b,c, IIIa,b,c and IVa,c) by oximation of Ia,b,c and their derivatives, their reaction mechanisms and configurations of the produced oximes.

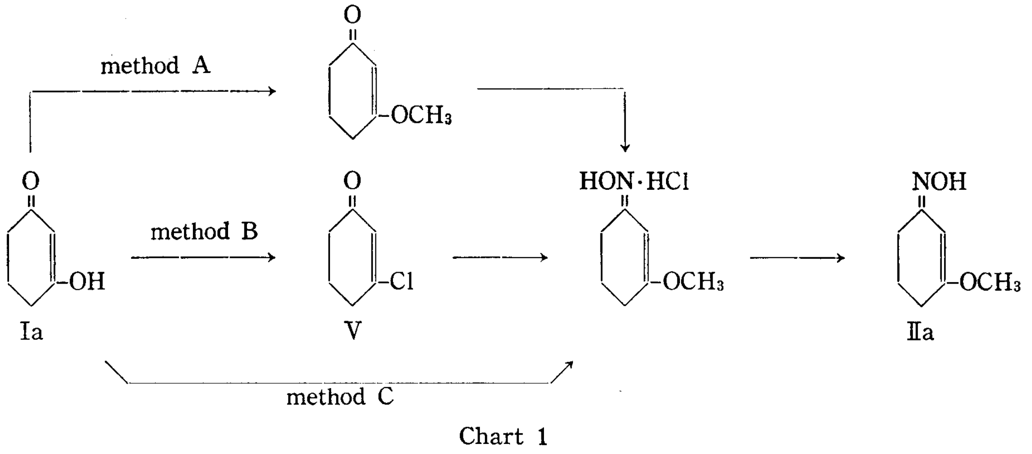

Chart 1

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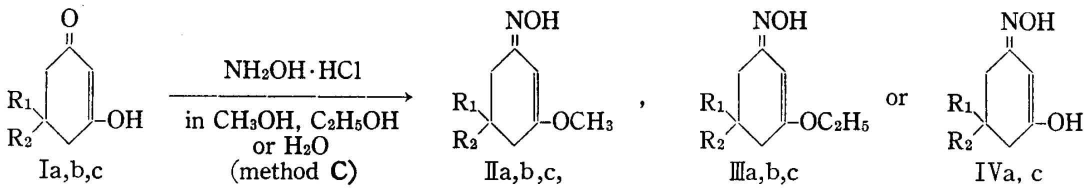
[1] Part I: Y. Tamura, Y. Kita, Y. Matsutaka and M. Terashima, *Chem. Ind.* (London), **1970, 1350.**

[2] Part of this work was reported at the 89 th, Annual Meeting of Pharmaceutical Society of Japan, Nagoya, April **1969.**

[3] Location: *6–5, Toyeyama, Toyonaka, Osaka.*

[4] W. Gittel, *Zeitschrift f. Naturwiss.*, **77**, 145 (1904).

The following three methods for preparing 3-methoxy-2-cyclohexen-1-one oxime (IIa) were investigated and compared. 3-Methoxy-2-cyclohexen-1-one,[5,6] prepared by alkylation of dihydroresorcinol (Ia), was treated with $NH_2OH \cdot HCl$ in methanol followed by neutralization with K_2CO_3 to give 3-methoxy-2-cyclohexen-1-one oxime (IIa) in 63% yield (method A). 3-Chloro-2-cyclohexen-1-one (V),[7] prepared from Ia with PCl_3, was treated with $NH_2OH \cdot HCl$ in methanol followed by neutralization with K_2CO_3 to give IIa in 61% yield (method B). Treatment of Ia with $NH_2OH \cdot HCl$ in methanol followed by neutralization with K_2CO_3 to give a 64% yield of IIa (method C). Comparison of the over all yields of IIa from Ia by method A, B, and C, which were 48%, 45% and 64%, respectively, indicated that method C was advantageous for the synthesis of IIa. When the oximation of Ia by method C was carried out in ethanol and water, 3-ethoxy-2-cyclohexen-1-one oxime (IIIa) and 3-hydroxy-2-cyclohexen-1-one oxime (IVa) were obtained in 59% and 51% yields, respectively. However, the same reaction in *tert*-BuOH gave IVa, as the only isolable product.



a: $R_1=R_2=H$, b: $R_1=H, R_2=CH_3$, c: $R_1=R_2=CH_3$

Chart 2

Nuclear magnetic resonance (NMR) and ultraviolet (UV) spectra allow a rapid and convenient determination of the *syn*- and *anti*-configuration of α,β-unsaturated ketoxime. It has been reported that in the NMR spectra of the α,β-unsaturated ketoximes the vinyl proton of *syn*-isomer shifts to lower field than that of *anti*-isomer[8] and in the UV spectra the *syn*-isomer exhibits maximum absorption at a longer wave length and with slightly less intensity than the *anti*-isomer.[9] The NMR spectra (in $CDCl_3$) of IIa and IIIa shows two singlet absorptions for the vinyl proton at τ 4.00—4.04 ascribed to the *syn*-isomer and at τ 4.63—4.80 ascribed to the *anti*-isomer. This indicates that these oximes exist in two forms. Further, from the integrated value of their vinyl protons, it is determined that IIa and IIIa are 2:1 and 4:3 mixtures of *syn*- and *anti*-isomers. Repeated fractional crystallizations of IIa and IIIa from water yielded the corresponding pure *syn*-oximes (IIa$_{syn}$ and IIIa$_{syn}$), but failed to yield the pure *anti*-oximes. Each of IIa$_{syn}$ and IVa$_{syn}$ shows a NMR spectrum lacking any detectable *anti*-absorptions. Both IIa$_{syn}$ and IIa (*syn*:*anti*=2:1) were converted to the same 3:2 mixture of *syn*- and *anti*-isomer by heating at 160° for 30 min (Fig. 1) but did not isomerize by treatment with 10% K_2CO_3 and also by alumina and silica gel column chromatographies.

A mechanism for the convertion of V into IIa by method B is proposed in Chart 3 from the examination of the progress of reaction by thin-layer chromatography (TLC); the oximation of V with $NH_2OH \cdot HCl$ occurs at first and then the replacement of β-chlorine atom with alkoxy group follows. The reaction of V and $NH_2OH \cdot HCl$ is very fast and, thus, after 5 min from the beginning of reaction, V has already disappeared from the reaction mixture and the hydrochlorides of the V oxime and IIIa appeared. With lapse of time, the former hydro-

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5) R. Grewe, E. Nolte and R. Rotzoll, *Chem. Ber.*, **89**, 600 (1956).

6) J.W. Ralls, W.C. Wildmann, K.E. McCaleb and A.L. Wilds, U.S. Patent 2674627 (1954) [*C. A.*, **49**, 1813c (1955)]; M. Bornstein, R. Pappo and J. Szmuskovicz, *Bull. Research Council Israel*, **2**, 273 (1952).

7) A.R. Crossley and H.R. LeSeuer, *J. Chem. Soc.*, **1903**, 160.

8) *a*) W.R. Benson and A.E. Pohland, *J. Org. Chem.*, **30**, 1129 (1965); *b*) R.H. Mazur, *J. Org. Chem.*, **26**, 1289 (1961); G. Slomp and W. Wechter, *Chem. Ind.* (London), **1962**, 42; Z.W. Wolkowski, N. Thoai and J. Wiemann, *Tetahedron Letters*, **1970**, 93.

9) S. Hara, K. Oka and Y. Ike, *Chem. Ind.* (London), **1967**, 832.

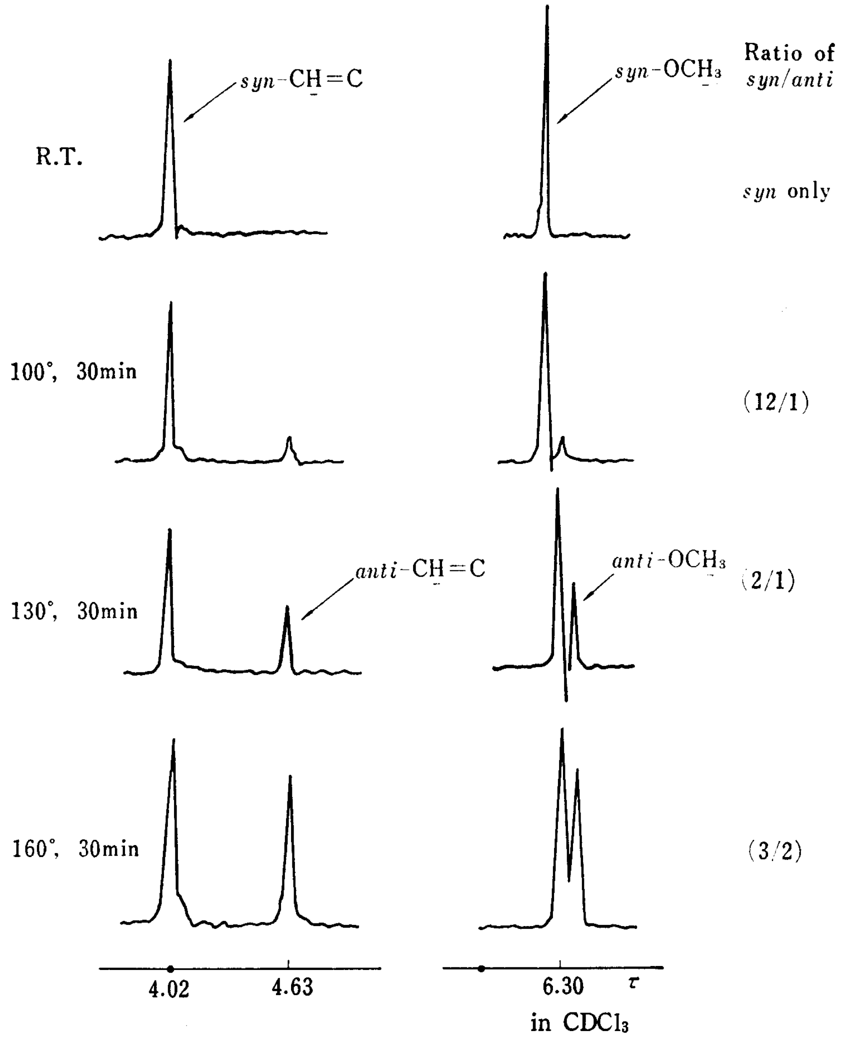

Fig. 1. Thermal Isomerization of IIa_{syn} into a Mixture of IIa_{syn} and IIa_{anti}

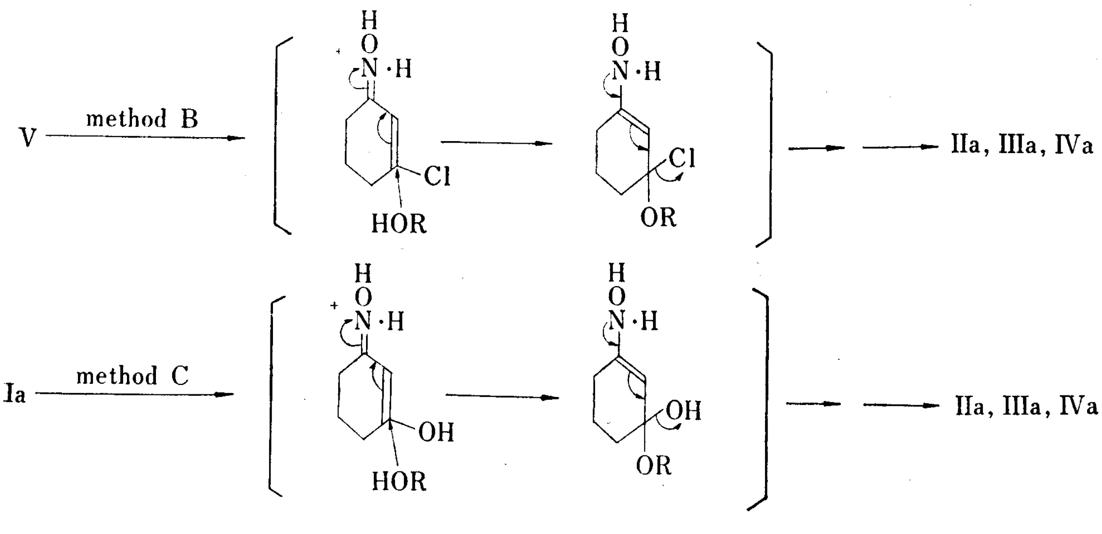

Chart 3

chloride gradually decreases and the latter hydrochloride increases, and after 45 min only the hydrochloride of IIIa is detectable. The method C from Ia to IIa is assumed to proceed similarly as shown in Chart 3. These mechanisms are supported by the following chemical evidence: treatment of the V oxime and the hydrochloride of IVa with $NH_2OH \cdot HCl$ in ethanol gave the IIIa hydrochloride in good yields.

Oximations of dihydroorcinol (Ib) and dimedone (Ic) were carried out by method C employed for the oximation of Ia. 3-Alkoxy-5-methyl- (IIb and IIIb), 3-alkoxy-5,5-dimethyl- (IIc and IIIc) and 3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one oximes (IVc) were obtained as mixtures of *syn*- and *anti*-isomers, whose configurations were determined by the NMR spectral analysis. These results are listed in Table I.

Table I. Yield and *syn-anti* Ratio of 3-Alkoxy-2-cyclohexen-1-one Oximes by Method C

Oximes			Reaction		*syn*/*anti* ratio	Chemical shift (τ)	
No.	R_1	R_2	Solvent	Yield (%)		*syn*	*anti*
IIa	H	H	CH_3OH	64	2/1	4.02	4.63
IIb	CH_3	H	CH_3OH	52	2/1	4.05	4.70
IIc	CH_3	CH_3	CH_3OH	65	5/4	4.03	4.69
IIIa	H	H	C_2H_5OH	59	4/3	4.02	4.68
IIIb	CH_3	H	C_2H_5OH	46	2/1	4.03	4.65
IIIc	CH_3	CH_3	C_2H_5OH	52	3/2	4.03	4.69

In a classic paper Gittel stated[4] that the treatment of Ic with $NH_2OH \cdot HCl$ in ethanol gave the amorphous monooxime of Ic, which was allowed to keep in conc. HCl to give the crystalline monooxime hydrochloride of Ic. From our experimental results, the former amorphous monooxime should be corrected to IIIc.

Experimental[10]

3-Methoxy-2-cyclohexen-1-one——i) Prepared according to the method of R. Grewe, E. Nolte and R. Rotzoll.[5] A solution of Ia (3.36 g), MeOH (20 ml), *p*-TsOH (0.150 g) and C_6H_6 (57 ml) was refluxed for 8 hr using a Dean-Stark water separator. The cooled reaction mixture was poured into water and extracted with C_6H_6. The extract was washed with 2% NaOH, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled under reduced pressure to give 1.85 g (49%) of 3-methoxy-2-cyclohexen-1-one as a colorless liquid, bp 61.5—63.5° (0.17 mm).

ii) Prepared from Ia with CH_2N_2 in ether in 76% yield.[6]

3-Methoxy-2-cyclohexen-1-one Oxime (IIa)——Method A: A solution of 3-methoxy-2-cyclohexen-1-one (1.29 g) and $NH_2OH \cdot HCl$ (0.720 g) in absolute MeOH (12 ml) was heated at 100° in an oil bath for 1 hr. The solution was concentrated *in vacuo* to give 1.75 g of a syrup. The syrup was taken up in CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was absorbed on a column of alumina (27 g). The column was treated successively with pet-ether (20 ml), C_6H_6 (50 ml), 90% C_6H_6–10% EtOAc (50 ml) and EtOAc (20 ml). Elution with 90% C_6H_6–10% EtOAc gave 0.920 g (63%) of IIa (*syn*: *anti*=2:1) as white crystals, mp 55—63°. IR γ_{max}^{KCl} cm^{-1}: 3170, 3050, 1630, 1610, 1020, 995, 960, 710 and 670. UV λ_{max}^{EtOH} $m\mu$ ($\log\varepsilon$): 249 (4.16). NMR (in $CDCl_3$) τ: 1.30 (1H, b-s, OH), 4.02 (2/3H, s, *syn*-vinyl proton), 4.63 (1/3H, s, *anti*-vinyl proton), 6.30 (2H, s, *syn*-OCH_3) and 6.35 (1H, s, *anti*-OCH_3). Distillate of IIa, mp 55—63°, under reduced pressure was subjected to a elemental analysis, bp 133—136° (8mm), mp 62.5—64.5°. *Anal.* Calcd. for $C_7H_{11}O_2N$: C, 59.55; H, 7.85; N, 9.92. Found: C, 59.34; H, 7.67; N, 10.20. Recrystallization of IIa (*syn*:*anti*=2:1) from water gave 0.420 g of pure *syn*-isomer (IIa_{syn}) as white crystals, mp 86.5—87.0°. IR γ_{max}^{KCl} cm^{-1}: 3170, 3050, 1630, 1610, 1020, 960 and 670. UV λ_{max}^{EtOH} $m\mu$ ($\log\varepsilon$): 251 (4.02). NMR (in $CDCl_3$) τ: 0.80 (1H, b-s, OH), 4.02 (1H, s, *syn*-vinyl proton) and 6.30 (3H, s, OCH_3). *Anal.* Calcd. for $C_7H_{11}O_2N$: C, 59.55; H, 7.85; N, 9.92. Found: C, 59.16; H, 7.56;

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10) All melting points were not corrected. The NMR spectra were measured with a Hitachi Perkin-Elmer H-60 type (60 Mc) spectrometer with tetramethylsilane as internal references and IR spectra on a Hitachi-EPI-G2 spectrophotometer.

N, 10.13. Fusion of IIa_{syn} at 100° for 30 min, at 130° for 30 min, at 160° for 30 min and at 180° for 30 min gave a 12:1 mixture of *syn*:*anti* (mp 75.5—78.5°), a 2:1 mixture of *syn*:*anti* (mp 59—61°) and a 3:2 mixture of *syn*:*anti* (mp 50—57°), respectively. Fusion of IIa (*syn*:*anti*=2:1) at 160° for 30 min gave a 3:2 mixture of *syn*:*anti* (mp 50—60°).

Method B: A solution of 3-chloro-2-cyclohexen-1-one (V; 1.54 g) and $NH_2OH \cdot HCl$ (0.820 g) in absolute MeOH (20 ml) was heated at 100° in an oil bath for 1 hr. The solution was concentrated *in vacuo* to give 1.36 g of a syrup. The syrup was treated in a similar manner to that described in method A. Yield of IIa was 1.01 g (61%), mp 57—67.5°. This material was identified with the sample of IIa prepared by method A by IR and TLC comparison.

Method C: A solution of Ia (33.6 g) and $NH_2OH \cdot HCl$ (20.8 g) in absolute MeOH (300 ml) was heated at 100° in an oil bath for 1.5 hr. The reaction mixture was concentrated *in vacuo* to give 49.0 g of a crude hydrochloride of IIIa as a syrup. The syrup was taken up in CH_2Cl_2, shaken with 10% K_2CO_3 and extracted with CH_2Cl_2. The insoluble solid was collected by filtration and washed with CH_2Cl_2 and water to give 1.86 g of a dioxime of Ia, mp 148—150° (lit.[11] 154°), which was identified with an authentic sample[11] by a mixed melting point determination and IR and TLC comparison. The CH_2Cl_2 extract was dried ($MgSO_4$) and concentrated *in vacuo* to give a crude IIa as a white crystalline mass, which was absorbed on a column of alumina (110 g). The column was treated successively with C_6H_6 (100 ml), 90% C_6H_6–10% EtOAc (550 ml), EtOAc (100 ml) and 90% EtOAc–10% MeOH (100 ml). Elution with 90% C_6H_6–10% EtOAc gave 26.9 g (64%) of IIa as white crystals, mp 56—63°. This material was identified with the sample of IIa prepared by method A by IR and TLC comparison.

3-Methoxy-5-methyl-2-cyclohexen-1-one Oxime (IIb)——Prepared from Ib (1.58 g) and $NH_2OH \cdot HCl$ (0.877 g) in MeOH (20 ml) by method C described for the preparation of IIa. Yeild of IIb was 0.913 g (52%). IIb (*syn*:*anti*=2:1), white crystals, mp 58—62°. This stuff gave a single spot in TLC on alumina with C_6H_6, C_6H_6:EtOAc=1:1, $CHCl_3$:EtOAc=3:1 and on silica gel with C_6H_6:EtOAc=1:2, $CHCl_3$:EtOAc=3:1, EtOAc, and did not show any detectable signals due to impurities other than IIb in its NMR spectrum. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3050, 1620, 1600, 1380, 1220, 1015, 980, 940 and 600. NMR (in $CDCl_3$) τ: 1.65 (1H, b-s, OH), 4.05 (2/3H, s, *syn*-vinyl proton), 4.70 (1/3H, s, *anti*-vinyl proton), 6.33 (2H, s, *syn*-OCH_3), 6.41 (1H, s, *anti*-OCH_3) and 8.92 (3H, b-s, C–CH_3). Distillate of IIb, mp 58—62°, under reduced pressure was subjected to an elemental analysis, bp 93—105° (0.03 mm, bath temp.), mp 91.5—109°. *Anal.* Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.68; H, 8.53; N, 8.87.

3-Methoxy-5,5-dimethyl-2-cyclohexen-1-one Oxime (IIc)——Prepared from Ic (21.0 g) and $NH_2OH \cdot HCl$ (10.4 g) in MeOH (100 ml) by method C described for IIa. Yield of IIc was 65%. IIc (*syn*:*anti*=5:4), pale yellow crystals, mp 47—71°: This stuff gave a single spot in TLC on alumina with C_6H_6:EtOAc=1:1, and did not show any detectable signals due to impurities other than IIc in its NMR spectrum. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3300, 1630, 1370, 1220, 1060, 1025, 1000, 980, 940 and 600. NMR (in $CDCl_3$) τ: 4.03 (5/9H, s, *syn*-vinyl proton), 4.69 (4/9H, s, *anti*-vinyl proton), 6.32 (5/3H, s, *syn*-OCH_3), 6.40 (4/3H, s, *anti*-OCH_3) and 8.98 (6H, s, di-CH_3). Distillate of IIc, mp 47—71°, under reduced pressure was subjected to an elemental analysis, bp 104—110° (0.07 mm, bath temp.), mp 52—67°. *Anal.* Calcd for $C_9H_{15}O_2N$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.89; H, 9.15; N, 8.02.

3-Ethoxy-2-cyclohexen-1-one Oxime (IIIa)——Prepared from Ia (22.4 g) and $NH_2OH \cdot HCl$ (14.0 g) in ethanol (200 ml) by method C described for IIa. Yield of IIIa was 59%. IIIa (*syn*: *anti*=4:3), white crystals, mp 68—87°. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3170, 3050, 1610, 1215, 1190, 970, 820 and 610. NMR (in $CDCl_3$) τ: 2.10 (1H, b-s, OH), 4.02 (4/7H, s, *syn*-vinyl proton), 4.68 (3/7H, s, *anti*-vinyl proton), 6.06 (2H, quartet, OCH_2) and 8.67 (3H, t, $CH_2C\underline{H}_3$). Distillate of IIIa (*syn*:*anti*=4:1) under reduced pressure was subjected to an elemental analysis, bp 93—95° (0.04 mm), mp 72—98°. *Anal.* Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.55; H, 8.54; N, 9.17. Recrystallization of IIIa (*syn*:*anti*=4:3) from water gave a pure *syn*-isomer (IIIa*syn*) as white crystals, mp 116—117.5° IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3150, 3040, 1635, 1610, 1215, 1190, 970, 810 and 610. NMR (in $CDCl_3$) τ: 1.20 (1H, b-s, OH), 4.02 (1H, s, *syn*-vinyl proton), 6.06 (2H, quartet, OCH_2) and 8.68 (3H, t, $CH_2C\underline{H}_3$). *Anal.* Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.63; H, 8.36; N,8.90.

3-Ethoxy-5-methyl-2-cyclohexen-1-one Oxime (IIIb)——Prepared from Ib (12.6 g) and $NH_2OH \cdot HCl$ (6.95 g) in ethanol (150 ml) by method C described for IIa. Yield of IIIb was 46%. IIIb (*syn*:*anti*=2:1), white crystals, mp 43—61°. This stuff gave a single spot in TLC on alumina with C_6H_6, C_6H_6:EtOAc=1:1, and did not show any detectable signals due to impurities other than IIIb in its NMR spectrum. IR $\nu_{\max}^{\mathrm{KCl}}$ cm^{-1}: 3200, 1630, 1610, 1380, 1340, 1210, 1040, 975 and 630. NMR (in $CDCl_3$) τ: 1.17 (1H, b-s, OH), 4.03 (2/3H, s, *syn*-vinyl proton), 4.65 (1/3H, s, *anti*-vinyl proton), 8.68 (3H, t, $CH_2C\underline{H}_3$) and 8.94 (3H, b-s,$CH_2C\underline{H}_3$). Distillate of IIIb, mp 43—61°, under reduced pressure was subjected to an elemental analysis, bp 110—116° (0.03 mm, bath temp.), mp 57—72°. *Anal.* Calcd. for $C_9H_{15}O_2N$: C, 63.88; H, 8.94; N, 8.28. Found: C, 64.14; H, 9.07; N, 8.14.

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[11] G. Merling, *Ann.*, **278**, 39 (1894).

3-Ethoxy-5,5-dimethyl-2-cyclohexen-1-one Oxime (IIIc)——Prepared from Ic (7.00 g) and $NH_2OH \cdot HCl$ (3.47 g) in ethanol (70 ml) by method C described for IIa. Yield of IIIc was 52%. IIIc (*syn*:*anti* $=3:2$), colorless syrup: This stuff gave a single spot in TLC on alumina with C_6H_6, C_6H_6:EtOAc$=1:1$, and did not show any detectable signals due to impurities other than IIIc in its NMR spectrum. IR ν_{max}^{KCl} cm^{-1}: 3300, 1630, 1370, 1225, 1060, 1025, 1000, 980, 940 and 600. NMR (in $CDCl_3$) τ: 4.03 (3/5H, s, *syn*-vinyl proton), 4.69 (2/5H, s, *anti*-vinyl proton), 6.32 (9/5H, s, *syn*-OCH_3), 6.40 (6/5H, s, *anti*-OCH_3) and 8.98 (6H, s, di-CH_3). Distillate of IIIc (*syn*:*anti*$=3:2$) under reduced pressure was subjected to an elemental analysis, bp 110—118° (0.05 mm, bath temp.). *Anal.* Calcd. for $C_{10}H_{17}O_2N$: C, 65.54; H, 9.35; N, 7.64. Found: C, 66.12; H, 9.09; N, 6.98.

3-Hydroxy-2-cyclohexen-1-one Oxime (IVa)——Prepared from Ia (3.92 g) and $NH_2OH \cdot HCl$ (2.44 g) in water (40 ml) by method C described for IIa. Yield of IVa was 2.27 g (51%). IVa, yellow crystals, mp 67—71°, bp 120—130° (0.02 mm, bath temp.): This stuff gave a single spot in TLC on silica gel with C_6H_6:EtOAc$=4:1$, C_6H_6:MeOH$=4:1$, C_6H_6:EtOAc:MeOH$=3:1:1$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3270, 1720, 1270, 960 and 655, ν_{max}^{KCl} cm^{-1}: 3200, 1600, 1550—1450, 1320, 1260, 1200, 1160, 1080, 1050, 980 and 600. UV $\lambda_{max}^{H_2O}$ mμ: 289. Recrystallization of IVa from water gave monohydrate of IVa, mp 78°. *Anal.* Calcd. for $C_6H_9O_2N \cdot H_2O$: C, 49.64; H, 7.64; N, 9.65. Found: C, 49.10; H, 7.49; N, 9.36.

3-Hydroxy-5,5-dimethyl-2-cyclohexen-1-one Oxime (IVc)——i) Prepared from Ic (5.20 g) and $NH_2OH \cdot HCl$ (2.58 g) in water(40 ml) by method C described for IIa. Yield of IVc was 2.84 g (49%). IVc, yellow crystals, mp 90—112°: This stuff gave a single spot in TLC on silica gel with C_6H_6:EtOAc$=1:1$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280, 1710, 1250, 1010 and 950, ν_{max}^{KCl} cm^{-1}: 3200, 1710, 1550—1510, 1340, 1260, 1160, 1060, 1020 and 970. UV $\lambda_{max}^{H_2O}$ mμ: 291. Recrystallization of IVc, mp 90—112°, from water gave yellow powder, mp 115°. This material was identified with the authentic sample, prepared according to the following method of W. Gittel,[4] in all respects.

ii) Prepared according to the method of W. Gittel[4]. A solution of Ic (5.20 g) and $NH_2OH \cdot HCl$ (2.50 g) in EtOH (50 ml) was refluxed for 2 hr and concentrated *in vacuo* to give a yellow-brown syrup (5.25 g). The syrup was added to C-HCl and allowed to stand at room temperature for 6 days. The separated crystals were collected by filtration and washed with a small amount of C-HCl to give the hydrochloride of IVc as colorless crystals, mp 125—150°. The hydrochloride was neutralized with 10%-NaOH, extracted with CH_2Cl_2, dried ($MgSO_4$) and concentrated *in vacuo* to give IVc as yellow crystals, mp 95—112°, Yield of IVc from Ia was 1.04 g (18%). Recrystallization from water gave yillow powder, mp 115° (lit.[4] 115°).

3-Chloro-2-cyclohexen-1-one (V)——Prepared according to the method of Crossley and LeSeuer.[7] Yield, 72%.

3-Chloro-2-cyclohexen-1-one Oxime——Prepared according to the method of W.R. Benson.[8a] To a solution of 3-chloro-2-cyclohexen-1-one (3.90 g) in EtOH (14 ml) was added a solution of $NH_2OH \cdot HCl$ (3.12 g) and AcONa (3.72 g) in H_2O (14 ml). The solution was refluxed for 1 hr and evaporated *in vacuo*. The residue was taken up in ether, washed with H_2O, dried ($MgSO_4$) and evaporated to give 2.75 g (64%) of a crystalline VIa, mp 61—65°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200, 1630, 1610, 1350, 1000, 950, 880 and 650. NMR (in $CDCl_3$) τ: 2.90 (4/11H, s, *syn*-vinyl proton), 3.77 (7/11H, s, *anti*-vinyl proton). Recrystallization from $MeOH-H_2O$ gave pure *anti*-oxime as white needles, mp 104°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200, 1630. UV λ_{max}^{EtOH} mμ: 240. NMR (in $CDCl_3$) τ: 1.35 (1H, b-s, OH), 3.77 (1H, s, *anti*-vinyl proton). *Anal.* Calcd. for C_6H_8ONCl: C, 49.49; H, 5.54; N, 9.62. Found: C, 49.33; H, 5.65; N, 9.71.

Formation of IIIa Hydrochloride——i) From 3-Chloro-2-cyclohexen-1-one Oxime (VIa): A mixture of VIa (100 mg, mp 61—65°) and $NH_2OH \cdot HCl$ (62 mg) in EtOH (1 ml) was heated in a water bath for 30 min. The reaction mixture was concentrated *in vacuo* to give a hydrochloride of IIIa, [mp 190—196° (decomp.), IR ν_{max}^{KCl} cm^{-1}: 3130, 2830, 2650, 1590, 1410, 1380, 1250, 1200, 1180, 1080, 1050, 1020, 940 and 840] in good yield, which was identified with a sample of the IIIa hydrochloride prepared by treatment of IIIa with EtOH-HCl.

ii) From 3-Hydroxy-2-cyclohexen-1-one Oxime (IVa): The hydrochloride of IVa (1.03 g) was heated under reflux in EtOH (10 ml) for 1 hr. The reaction mixture was concentrated *in vacuo* and the residue was triturated with EtOH-ether to give 1.04 g of the IIIa hydrochloride. This compound was identified with the sample prepared in i).