# Alkylation of Ketoxime with Dichloromethane Using Bases under Phase-transfer Conditions. Formation of Methylene Dioxime and Novel Heteromacrocyclic Compounds

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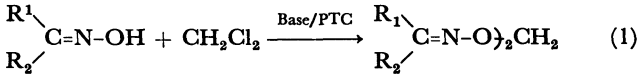
Ketoximes, when treated with $KO_2$ (1 equiv) in the presence of di-$\mu$-chlorobis(2-methylallyl)dipalladium-(II) (0.1 equiv per Pd) in dichloromethane, give methylene dioximes in moderate yields. This alkylation of ketoximes with $CH_2Cl_2$ is also promoted by the use of potassium carbonate in the presence of phase-transfer catalysts such as 18-crown-6. Study on the reactivity of a series of ketoximes in these reactions shows that proton abstraction by base is a crucial step in the latter reaction. By contrast, in the former system the reactivity is supposed to be controlled by nucleophilicity of the oximate anion coordinated to palladium(II). Application of the present reaction to (*E,E*)-1,2-diketone dioxime such as dimethylglyoxime leads to the formation of novel 21-membered ring heteromacrocyclic compounds in which oxime units are sequentially linked by methylene bridge.

Previously we have reported palladium-induced deoximation[1] and Beckmann fragmentation of ketoximes[2] by the use of peroxobis(triphenylphosphine)palladium(II), $(PPh_3)_2Pd\langle^{O}_{O}$. During the course of the studies, we have found that the alkylation of ketoximes (**1**) with dichloromethane is promoted by $KO_2$ in the presence of palladium(II) catalyst to give methylene dioximes (**2**) of a novel class of compounds.[3] Since the reaction is one of the rare examples of the use of dichloromethane as both solvent and electrophile,[4] we have studied this type of reactions in detail.

Use of a simple base such as potassium carbonate in combination with a phase-transfer agent such as 18-crown-6 has promoted the reaction as well. However,



(1)

**1** **2**

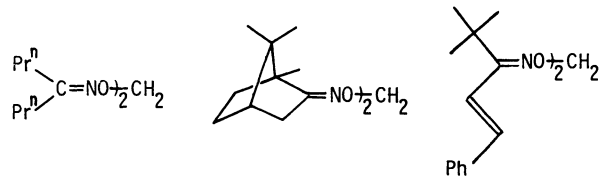
PTC: Phase-Transfer Catalyst

interestingly, these two systems have shown an inverse reactivity toward aryl and alkyl ketoximes.

Application of the reaction to 1,2-diketone dioximes, *e.g.*, dimethylglyoxime, has led to the synthesis of a novel heteromacrocyclic compound formed *via* a sequential oligomerization of the dioxime and dichloromethane. Although a variety of macrocyclic polyether and azacrown compounds have been reported in literatures,[5] there are few examples of heteromacrocycles containing oxime linkages. These are Vögtle's macrocyclic mono- and dioximes[6] prepared from 1,2-diketone dioximes and 1,$\omega$-dichlorooligo-1-oxapropane $[Cl\{CH_2CH_2O\}_nCH_2CH_2Cl]$[7] and Sarlo's macrocyclic polyhydroximates formed *via* nucleophilic polymerization of acetonitrile oxide.[8] There has been, however, no precedent for the dioxime crowns such as **11** (*vide infra*) in which oxime units are sequentially linked by methylene bridges. This paper describes the alkylation of ketoximes with dichloromethane under phase-transfer conditions leading to the formation of methylene dioximes and dioxime crowns.

## Results and Discussion

*Reaction of Ketoximes with $CH_2Cl_2$* In the present study, ketoximes (**1**) have been generally allowed to react with an equimolar amount of $KO_2$ in dichloromethane in the presence of $[(2\text{-methylallyl})PdCl]_2$ (**3**) (0.1 equiv per Pd). Under the conditions, a relatively wide range of ketoximes, *e.g.*, 4-heptanone oxime, *d*-camphor oxime, and (*Z*)-2,2-dimethyl-5-phenyl-4-penten-3-one oxime, give the corresponding methylene dioximes (**2a**), (**4**), and (**5**) in moderate

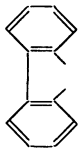


**2a** **4** **5**

yields (23—53%). If 2 equiv of $KO_2$ was used, the yields increased up to 60—96%. However, if $KO_2$ alone was used, entirely no reaction took place. Use of other palladium(II) complexes such as $PdCl_2(CH_3CN)_2$ and $Pd(OAc)_2$ as the catalyst also led to the alkylation of ketoximes. Since $KO_2$ is insoluble in dichloromethane, palladium(II) complexes are considered to act as a phase-transfer agent.

In this system, aryl ketoximes such as benzophenone oxime gave no appreciable amount of the alkylation product. By contrast, when the aryl ketoximes were treated with potassium carbonate (1.1 equiv) in dichloromethane containing 18-crown-6 (0.1 equiv), the corresponding methylene dioximes were formed in good yield (*e.g.*, 80% yield with benzophenone oxime).

Table 1. Formation of methylene dioximes **2** from a series of ketoximes **1**

| Entry | Ketoxime **1** | | | Yield of methylene dioxime **2**/% | | | |
|---|---|---|---|---|---|---|---|
| | $R_1$ | $R_2$ | | $KO_2$/Pd complex **3**[a] | $K_2CO_3$/18-c-6[b] | $KO_2$/18-c-6[b] | $Bu^tOK$/18-c-6[b] |
| 1 | $C_3H_7$ | $C_3H_7$ | (**1a**) | 53 (96)[c] | 0 | | |
| 2 | $CH_3$ | $CH_3$ | (**1b**) | 45 | 0 | 27 | 74 |
| 3 | $-(CH_2)_5-$ | | (**1c**) | 39 | 0 | | |
| 4 | $PhCH_2CH_2$ | $PhCH_2CH_2$ | (**1d**) | 36 | 19 | | |
| 5 | $PhCH_2$ | $PhCH_2$ | (**1e**) | 24 | 65 | | (66)[a] |
| 6 | Ph | Ph | (**1f**) | 7 | 83 (72)[a] | 66 | 76 |
| 7 |  | | (**1g**) | 2 | 90 | | |
| 8 | PhCO | Ph (*E*) | (**1h**) | 0 | 92 | | |

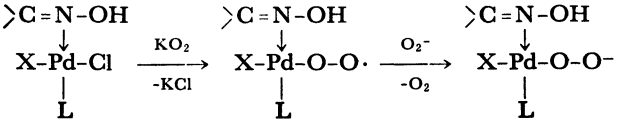
a) Isolated yield. b) In this system, yields were determined by $^1H$ NMR spectroscopy. c) Isolated yield when 2 equiv of $KO_2$ was used.

These results prompted us to examine the difference in reactivity between the two reaction systems using a series of ketoximes. From Table 1, it can be seen that in the former system aliphatic ketoximes afford higher yields of methylene dioxime than aryl ketoximes, whereas the opposite trend is observed in the latter ($K_2CO_3$/18-c-6). Further, the reactivities observed in both systems appear to change as a function of the p*K*a of ketoximes.[9]

Although potassium carbonate serves as an efficient, strong base in the presence of solid-liquid two phase catalysis,[10] it is not much basic as to promote the reaction with less acidic aliphatic ketoximes such as **1b** (Entries 1—3, Table 1). When $K_2CO_3$ was replaced with more basic $Bu^tOK$, the aliphatic ketoxime **1b** gives methylene dioxime **2b** in a good yield (74%). The use of $KO_2$ with 18-crown-6 gives **2b** only in 27% yield in accordance with the order of decrease in basicity ($Bu^tOK > KO_2 > K_2CO_3$).[11] Therefore, it is evident that proton abstraction from the oxime by base is a crucial step in this system. Note that there have been ample examples that $KO_2$ acts as a Br$\phi$nsted base in the presence of phase-transfer agents.[12]

In the $KO_2$–Pd(II) system, more acidic ketoximes such as (**1d**)—(**1f**) led to the formation of palladium(II) complexes containing oximate ligands in 15—27% yield (based on Pd), along with the alkylation products. The complexes are formulated as $[(R_2C{=}NO)_2(R_2C{=}NOH)_2]Pd$ (**6**) by comparing the spectra data with those of the authentic complex **6a** (R= $CH_2Ph$) prepared from $Pd(acac)_2$ and dibenzyl ketone oxime.[13] Thus, when the oxime has lower p$K_a$, its anion is thought to successively coordinate to Pd(II) and has no nucleophilic ability enough to attack at the methylene carbon of dichloromethane.

The formation of methylene dioximes **2** is readily accounted for by succesive, nucleophilic displacement of an oximate anion to dichloromethane. In the former system ($KO_2$/Pd(II)), the oximate anion is probably formed *via* the following steps. At first, coordination of the nitrogen atom to Pd(II) complex takes place in dichloromethane solution. Superoxide anion ($O_2^{\cdot-}$) is then transfered into the organic phase *via* anion exchange (**7**→**8**) with the chloride ligand of Pd(II) complex. Electron transfer (**8**→**9**) followed by proton abstraction[14] results in the formation of oximate anion in the coordination sphere of palladium(II). Alternatively, the oximate anion may be

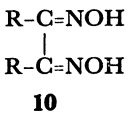



**7** **8** **9**

directly formed from the coordinated oxime **7** by the action of $KO_2$ with releasing HOO·. In any case, depending on its nucleophilicity, the oximate anion thus produced attacks at the methylene carbon of $CH_2Cl_2$.[15] Since less acidic ketoximes readily undergo the reaction in this system, the acidity of oximes must be enhanced by its coordination to palladium(II).

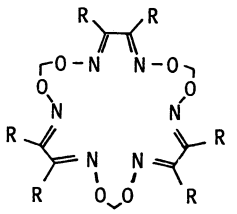
*Reaction of 1,2-Diketone Dioxime with $CH_2Cl_2$.* Application of the present methods to 1,2-diketone dioximes (**10**) resulted in either formation of nitractable palladium complexes ($KO_2$/Pd(II)) or recovery of the starting materials ($K_2CO_3$/18-c-6). However, the use of $Bu^tOK$ in the presence of 18-crown-6 led to a successful synthesis of novel dioxime crown compounds containing methylene linkages such as **11**.

The procedure for the synthesis of 21-membered ring compound **11a** is simple. To a suspended solution of (*E*,*E*)-2,3-butanedione dioxime (**10a**), $Bu^t$ OK (2 equiv) and 18-crown-6 (0.1 equiv) in THF was slowly added an excess of dichloromethane, and the mixture



**10**

| | Conf. | R |
|---|---|---|
| **a**; | (*E*,*E*) | Me |
| **b**; | (*E*,*E*) | Pr$^i$ |
| **c**; | (*E*,*E*) | Pr$^n$ |
| **d**; | (*E*,*E*) | Ph |
| **e**; | (*E*,*E*) | R,R=-(CH$_2$)$_4$- |
| **f**; | (*Z*,*Z*) | Cyclohexyl |
| **g**; | (*Z*,*Z*) | Pr$^i$ |
| **h**; | (*Z*,*E*) | Pr$^i$ |

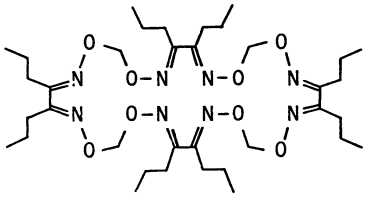


**11**

**a**; R=Me
**b**; R=Pr$^i$

was refluxed. After filtration of the reaction mixture and evaporation of the solvent and excess $CH_2Cl_2$, the residue was thoroughly washed with methanol to remove unreacted oxime **10a**. The remaining solid was recrystallized from MeOH–THF to give **11a** in 20% yield as colorless crystals. In the absence of 18-crown-6, no reaction takes place. However, the use of trioctylmethylammonium chloride (Capriquat) as a phase-transfer agent is comparatively effective in promoting the reaction. If THF is not used as the co-solvent, the yield of **11a** is reduced to ≈2%. A poor yield (4%) of **11a** is also resulted, when **10a** was treated with aqueous 20% NaOH solution in the presence of tetrabutylammonium hydrogensulfate (0.1 equiv) in $CH_2Cl_2$.

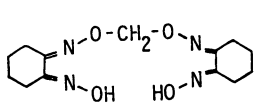
The same type of dioxime crown **11b** was obtained from (*E*,*E*)-2,5-dimethyl-3,4-hexanedione dioxime (**10b**) (R=Pr$^i$) in 21% yield by the same treatment (Bu$^t$OK/18-c-6). By contrast, (*E*,*E*)-dioxime **10c** of R=Pr$^n$ gave **12**, in which four oxime units are linked by methylene bridges, in 40% yield.



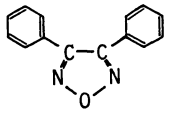
**12**

In the $^1$H NMR spectra of **11a**, **11b**, and **12**, the -OCH$_2$O-protons appear as a singlet approximately at $\delta$ 5.50, and their $^{13}$C{$^1$H} NMR spectra ($CDCl_3$) also exhibit only singlet due to the methylene carbon at $\delta$ 99.45 ppm for **11a** and $\delta$ 99.31 ppm for **12** relative to $Me_4Si$. These results indicate the equivalence of all the -OCH$_2$O- groups. In addition, the signal of alkyl substituent (R=Me, Pr$^i$, and Pr$^n$) in each compound has been shown to be magnetically equivalent (*vide infra*). These data also support the structures as illustrated above. The extent of oligomerization was determined by the mass spectra of the products.

Although (*E*,*E*)-dioximes appear to generally undergo the present sequential oligomerization, it is not the case for **10e** (R,R=-(CH$_2$)$_4$-) and **10d** (R=Ph). Thus, (*E*,*E*)-1,2-cyclohexanedione dioxime (**10e**) gave



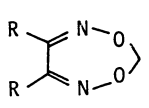
**13**



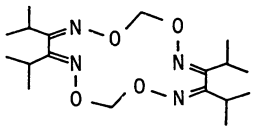
**14**

a 12% yield of **13**, a 2:1 adduct of the dioxime and $CH_2Cl_2$. (*E*,*E*)-benzil dioxime **10d** gave a 27% yield of 3,4-diphenylfurazan **14** formally *via* (*E*,*E*) $\rightleftarrows$ (*Z*,*E*) isomerization followed by dehydration.

As expected, the (*Z*,*Z*)-dioximes **10f** and **10g** do not undergo the present oligomerization, but intramolecular cyclization of a 1:1 adduct of the dioxime and $CH_2Cl_2$ takes place. Thus, **10f** (R=cyclohexyl) gave a 66% yield of 7*H*-3,4-dicyclohexyl-1,6,2,5-dioxadiazepine (**15a**), which is a previously unknown class of heterocyclic compounds. Similarly, (*Z*,*Z*)-dioxime **10g** afforded **15b** in 47% yield. In this case, a small amount (*ca.* ≈5%) of cyclic compound **16** containing



**15**



**16**

**a**; R=Cyclohexyl
**b**; R=Pr$^i$

two (*Z*,*E*)-oxime units was formed. The (*Z*,*E*)-configuration of this compound was assigned since the methyl signal of the two isopropyl group appears at different chemical shifts as two sets of doublets in its $^1$H NMR spectrum.

The (*Z*,*E*)-dioxime **10h** (R=Pr$^i$) also gave the dioxadiazepine **15b** in 16% yield, but the expected product **16** was not formed. In any case, when the substituent is Pr$^i$, (*Z*,*E*) $\rightleftarrows$ (*Z*,*Z*) isomerization of the oxime group takes place during the reaction.

## Experimental

*General.* NMR spectra were recorded on a 60-MHz Model JNM-MH-60 (Jeol) spectrometer; chemical shifts ($\delta$) expressed in parts per million relative to $Me_4Si$. IR spectra were recorded on a Hitachi 215 spectrometer. Mass spectra were taken on a Hitachi RSM-4 mass spectrometer. Elemental analyses were determined on a Yanagimoto MT-2 CHN recorder. Potassium superoxide was obtained from Ventron, ground to a fine powder in a Ar-filled drybag, and stored in a desiccator prior to use. Di-$\mu$-chlorobis(2-methylallyl)-dipalladium(II)[16] (**3**), palladium acetate(II),[17] bis(benzonitrile)dichloropalladium(II)[18] were prepared as the reported procedures. Dichloromethane was distilled from calcium hydride under argon or nitrogen. Ketoximes **1a-g** were prepared from the corresponding ketones according to the reported procedure. (*E*)-Benzil monoxime **1h** was prepared by the method of Taylor and Marks.[19] *d*-Camphor oxime, (*E*,*E*)-2,3-butanedione dioxime **10a** (dimethylglyoxime), (*E*,*E*)-benzil dioxime (**10d**), and (*E*,*E*)-1,2-cyclohexanedione dioxime (**10e**) are commercially available.

Three configurational isomers of (*E,E*)-**10b**, (*Z,Z*)-**10f**, and (*Z,E*)-**10h** were prepared from the oximation of 2,5-dimethyl-3,4-hexanedione. (*E,E*)-4,5-Octanedione dioxime (**10c**) and (*Z,Z*)-1,2-dicyclohexylethanedione dioxime (**10f**) were also prepared from the corresponding diketones. These details are described below.

*2,5-Dimethyl-3,4-hexanedione Dioxime (10b, g, and h).* To a solution of hydroxylamine hydrochloride (2.433 g, 0.035 mol) in 10 mL of water was added a soluton of 85% potassium hydroxide (2.307 g, 0.035 mol) in 6 mL of water in an ice bath. Into the cold solution was added 2,5-dimethyl-3,4-hexanedione[20] (1.990 g, 0.014 mol). The reaction mixture was stirred at 0 °C for 2 h and then at reflux for 2 h. After extraction with ether (10 mL×3), the extract was washed with water, shaken with brine, and dried over anhydrous magnesium sulfate. Concentration of the solvent followed by Kugelrohr distillation (55—60 °C/3 mmHg) (1 mmHg=133.322 Pa) gave 2,5-dimethyl-3,4-hexanedione monoxime (1.466 g, 67%). To a solution of the monooxime (1.415 g, 9.0 mmol) in 8 mL of 95% ethanol was added a solution of hydroxylamine hydrochloride (0.639 g, 9.2 mmol) and sodium acetate (1.292 g, 15.8 mmol) in 4 mL of water. The reaction mixture was refluxed for 4 h, and concentrated until the mixture became turbid, and then allowed to cool to room temperature. The white crystals were collected, washed thoroughly with water, and dried *in vacuo* at 50 °C. The crystals were found to contain three configurational isomers of the dioxime. Recrystallization from ether-petroleum ether afforded (*Z,Z*)-2,5-dimethyl-3,4-hexanedione dioxime **10g** (33%): mp 139—142 °C; IR (Nujol) 3260 (OH), 1100, 1048, 880, 715 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$=0.73 (12H, d, $J$=7 Hz, $-CH_3$), 2.17 (2H, heptet, $J$=7 Hz, >CH), 10.28 (2H, s, -OH). From the mother liquid, (*E,E*) and (*Z,E*)-isomers were separated by preparative TLC ($SiO_2$, ethyl acetate:hexane=3:7) in 2% and 6% yields, respectively. (*E,E*)-2,5-dimethyl-3,4-hexanedione dioxime (**10b**): $R_f$ 0.45; IR (Nujol) 3250 (OH), 1155, 1102, 1060, 990, 970, 912, 845, 745 $cm^1$; $^1H$ NMR (DMSO-$d_6$) $\delta$=1.05 (12H, d, $J$=7 Hz, $-CH_3$), 2.30 (2H, heptet, $J$=7 Hz, >CH), 10.78 (2H, s, -OH). (*Z,E*)-2,5-Dimethyl-3,4-hexanedione dioxime (**10h**): $R_f$ 0.29; IR (Nujol) 3240 (OH), 1167, 1150, 1035, 1012, 932 895, 861, 742 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$=0.99 (d, $J$=7 Hz, $-CH_3$, 6H), 1.03 (d, $J$=7 Hz, $-CH_3$, 6H), 2.30 (m, >CH, 2H), 10.48 (s, -OH, 1H), 10.77 (s, -OH, 1H). The configuration assignment of these dioximes were made on the basis of their $^1H$ NMR signals of OH proton in DMSO-$d_6$, according to the method of Tanaka and Shinra.[21]

*(E,E)-4,5-Octanedione Dioxime (10c).* The oximation of 4,5-octanedione[20] by the similar manner as above gave (*E,E*)-4,5-octanedione dioxime (**10c**) as the sole product; mp 178—179.5 °C; IR (Nujol) 3220 (OH), 1150, 1042, 1020, 922, 893, 872, 761 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$=0.70 (6H, m, $-CH_3$), 1.00—1.60 (4H, m, $-CH_2-$), 2.38 (4H, m, $-C(=N)-CH_2-$), 11.13 (2H, s, -OH). The (*E,E*)-configuration was assigned by the same method as above.

*(Z,Z)-1,2-Dicyclohexylethanedione Dioxime (10f).* The oximation of 1,2-dicyclohexylethanedione[20] by the similar manner as above gave the title compound as the sole product; mp 200 °C; IR (Nujol) 3250 (OH), 1115, 995, 960, 948, 893, 819, 810, 715 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$=0.91—2.46 (20H, m, $-CH_2-$), 10.28 (2H, s, -OH). The configuration assignment of the dioxime was made similarly as above.

*Reaction of Ketoximes with Dichloromethane in the Presence of $KO_2$ and 3. General Procedure.* In a drybag filled with argon, finely powdered potassium superoxide (4 mmol) was weighed and placed in a 100 mL flask containing a Teflon-coated magnetic stirrer bar, di-$\mu$-chlorobis(2-methylallyl)dipalladium (**3**, 0.079 g, 0.2 mmol) and ketoxime (**1**, 4 mmol). Into the flask was added 40 mL of dichloromethane, and the reaction mixture was stirred for 72 h at room temperature under argon. After the resulting potassium chloride was removed by filtration, the filtrate was concentrated under reduced pressure. The products were separated by means of $Al_2O_3$ column chromatography. Generally, elution with a 7:3 mixture of hexane and ethyl acetate gave the methylene dioxime **2**. Unreacted ketoximes were recovered from further elution with ether or methanol. Analytically pure methylene dioximes were obtained by recrystallization or distillation. The results are summarized in Table 1. Spectral and anaiytical data of the methylene dioximes **2** obtained in this system are described below.

*Methylene Dioxime 2a*: Bp 108—109 °C/3 mmHg; IR (neat) 1630 (C=N), 1146, 1005 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=0.92 (12H, t, $J$=7 Hz, $-CH_3$), 1.48 (8H, m, $-CH_2-$), 2.13 (8H, q, $J$=7 Hz, $-CH_2C=N-$), 5.37 (2H, s, $-OCH_2O-$). Found: C, 66.58; H, 11.38; N, 10.36%. Calcd for $C_{15}H_{30}N_2O_2$: C, 66.62; H, 11.18; N, 10.10%.

*Methylene Dioxime 2b*: Mp 39 °C; IR (Nujol) 1640 (C=N), 1150, 1020 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=1.80 (12H, s, $-CH_3$,), 5.30 (2H, s, $-CH_2-$). Found: C, 53.04; H, 8.92; N, 17.85%. Calcd for $C_7H_{14}N_2O_2$: C, 53.14; H, 8.91; N, 17.71%.

*Methylene Dioxime 2c*: Mp 47—48.5 °C; IR (Nujol) 1645 (C=N), 1135, 1020 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=1.60 (12H, m, $-CH_2-$), 2.18 (4H, m, $-CH_2-$), 2.47 (4H, m, $-CH_2-$), 5.37 (2H, s, $-OCH_2O-$). Found: C, 65.75; H, 9.41; N, 11.49%. Calcd for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.31; N, 11.76%.

*Methylene Dioxime 2d*: Mp 73 °C; IR (Nujol) 1628 (C=N), 1150, 1028 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=2.20—3.03 (16H, m, $-CH_2-$), 5.71 (2H, s, $-OCH_2O-$), 7.03—7.40 (20H, m, aromatic). Found: C, 81.27; H, 7.38; N, 5.42%. Calcd for $C_{35}H_{38}N_2O_2$: C, 81.04; H, 7.38; N, 5.40%.

*Methylene Dioxime 2e*: Mp 102 °C; IR (Nujol) 1630 (C=N), 1148, 1024 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=3.43 (4H, s, $-CH_2-$), 3.63 (4H, s, $-CH_2-$), 5.80 (2H, s, $-OCH_2O-$), 7.00—7.27 (20H, m, aromatic). Found: C, 80.71, H, 6.55; N, 6.10%. Calcd for $C_{31}H_{30}N_2O_2$: C, 80.49; H, 6.54; N, 6.06%.

*Methylene Dioxime 2f*: Mp 90—91 °C IR (Nujol) 1150, 1020 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=5.70 (2H, s, $-CH_2-$), 7.10—7.60 (20H, m, aromatic). Found: C, 79.99; H, 5.32; N, 6.79%. Calcd for $C_{27}H_{18}N_2O_2$: C, 79.78; H, 5.46; N, 6.89%.

*Methylene Dioxime 2g*: Mp 211—211.5 °C; IR (Nujol) 1620 (C=N), 1021 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=6.20 (2H, s, $-CH_2-$), 7.10—7.93 (14H, m, aromatic), 8.00—8.37 (2H, m, aromatic). Found: C, 80.86; H, 4.35; N, 7.30%. Calcd for $C_{27}H_{22}N_2O_2$: C, 80.58; H, 4.51; N, 6.96%.

*Methylene Dioxime 2h*: Mp 99—100 °C; IR (Nujol) 1679 (C=O), 1668 (C=N), 1035 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=5.76 (2H, s, $-CH_2-$), 7.03—8.03 (20H, m, aromatic). Found: C, 75.40; H, 4.72; N, 6.16%. Calcd for $C_{26}H_{22}N_2O_4$: C, 75.31, H, 4.79; N, 6.06%.

*Methylene Dioxime 4*: Yield 32%; mp 68 °C; IR (Nujol) 1675 (=N), 1005 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=0.77 (6H, s, $-CH_3$), 0.90 (6H, s, $-CH_3$), 1.00 (6H, s, $-CH_3$),

1.07—2.73 (14H, m, $-CH_2-$, and $\rangle CH$), 5.38 (2H, s, $-OCH_2O-$). Found: C, 72.50; H, 9.83; N, 7.82%. Calcd for $C_{21}H_{34}N_2O_2$: C, 72.79; H, 9.89; N, 8.09%.

*Methylene Dioxime* **5**: Yield 23%; bp 185 °C/0.15 mmHg; IR (neat) 1615 (C=N), 1245, 1075 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.36 (18H, s, $-Bu^t$), 6.30 (2H, s, $-CH_2-$), 7.15—7.48 (10H, m, =CH- and aromatic), 7.58—7.80 (4H, m, =CH- and aromatic).

The use of $Pd(OAc)_2$ or $PdCl_2(PhCN)_2$ in place of [(2-methylallyl)PdCl]$_2$ (**3**) in the reaction of **1b** (R=$CH_3$) under the conditions described above also gave the methylene dioxime **2b**. The isolable yield of **2b** were 42% with $Pd(OAc)_2$ and 34% with $PdCl_2(PhCN)_2$. In the reaction using 2 equiv of $KO_2$ under otherwise the same conditions as above, the methylene dioximes **2a** and **4** were isolated in 96% and 61% yield from **1a** and *d*-camphor oxime, respectively.

*Formation of Oximate Palladium(II) Complexes* **6**. The general procedure described above was followed by using 1,3-diphenyl-2-propanone oxime (**1e**, 0.901 g, 4 mmol), $KO_2$ (0.284 g, 4 mmol), di-$\mu$-chlorobis(2-methylallyl)dipalladium(II) (0.079 g, 0.2 mmol) and 40 mL of $CH_2Cl_2$. Alumina column chromatography ($Al_2O_3$, 18 g) of the reaction mixture gave the methylene dioxime **2e** (0.219 g, 24%) from the elution of hexane and ethyl acetate (7:3, 20 mL). Further elution with ethyl acetate gave unreacted **1e** (0.429 g, 48%). The oximate complex **6a** (R=$CH_2Ph$), (0.060 g, 15% based on Pd) was obtained from $CH_2Cl_2$ elution. Recrystallization from $CH_2Cl_2$ and petroleum ether afforded analytically pure **6a**: mp 145—147 °C; IR (Nujol) 1600, 1590, 1095, 1074, 1055, 1030, 742, 695 $cm^{-1}$; $^1H$ NMR ($CD_2Cl_2$–$CDCl_3$) $\delta$=2.83—4.13 (16H, m, $-CH_2-$), 6.77—7.03 (40H, m, aromatic) Found: C, 71.68; H, 5.72; N, 5.63%. Calcd for $C_{60}H_{58}N_4O_4Pd$: C, 71.68; H, 5.81; N, 5.57%.

The same reaction with **1d** (0.506 g, 2 mmol) gave the oximate complex **6b** (R=$CH_2CH_2Ph$), (0.061 g, 27% based on Pd), along with methylene dioxime **2d** (0.188 g, 36%). **6b**: mp 151 °C (decomp) IR (Nujol) 1602, 1580, 1157, 1090, 1030 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=2.75 (32H, m, $-CH_2-$), 7.00—7.37 (40H, m, aromatic). Found: C, 73.07; H, 6.67 N, 5.06%. Calcd for $C_{68}H_{74}N_4O_4Pd$: C, 73.07; H, 6,67; N, 5.01%.

Benzophenone oxime (**1f**) also gave this type of complex. However, no attempt to isolate the complex in a pure state was made, owing to its difficulty in the separation from unreacted ketoxime **1f**.

*Preparation of Complex* **6a** *(R=$CH_2Ph$).* A solution of $Pd(acac)_2$ (0.219 g, 0.72 mmol) and ketoxime **1e** (0.885 g, 3.9 mmol) in dichloromethane (5 mL) was stirred at room temperature for 0.5 h. After removal of the solvent, recrystallization ($CH_2Cl_2$–hexane) of the resulting complex gave 0.825 g of the complex **6a** (86%), whose spectral data were identical with those of the aforementioned complex.

*Reaction of Ketoximes with Dichloromethane in the Presence of $K_2CO_3$ and 18-Crown-6. General Procedure.* In a 25 mL flask containing a Teflon-coated magnetic stirrer bar were placed the oxime (1.0 mmol), potassium carbonate (0.152 g, 1.1 mmol), and 18-crown-6 (0.026 g, 0.1 mmol). Into the flask was then added 10 mL of dichloromethane (distilled from $CaH_2$), and the reaction mixture was refluxed for 12 h under argon with stirring. After the resulting potassium chloride was removed by filtration, the filtrate was concentrated under reduced pressure. The residues which contain the methylene dioxime and/or unreacted oxime were analyzed by $^1H$ NMR spectroscopy to determine the product yield. Results are also shown in Table 1.

A typical experiment in this system is described as followed. A mixture of oxime **1f** (0.197 g, 1 mmol), $K_2CO_3$ (0.152 g, 1.1 mmol), and 18-crown-6 (0.026 g, 0.1 mmol) in $CH_2Cl_2$ (10 mL) was refluxed for 12 h with stirring. After work-up as decribed above, NMR analysis of the reaction mixture showed the presence of methylene dioxime **2f** in 83% yield with 17% of unreactive oxime. The reaction mixture was then chromatographed on alumina column (12 g) to give methylene dioxime **2f** (0.157 g, 72%) from the elution with 20 mL of petroleum ether and 25 mL of ether.

*3,4,10,11,17,18-Hexamethyl-1,6,8,13,15,20-hexaoxa-2,5,9,12,16,19-hexaazahenicosa-2,4,9,11,16,18-hexaene (**11a**).* In a 300 mL of flask containing a Teflon-coated magnetic stirrer bar were placed (*E,E*)-2,3-butanedione dioxime **10a** (3.832 g, 33 mmol), $Bu^tOK$ (7.406 g, 66 mmol) and 18-crown-6 (0.872 g, 3.3 mmol), and into the flask was added THF (100 mL). To the resulting suspended solution was added dichloromethane (100 mL) such a rate to maintain a gentle reflux with stirring. After the addition was complete, the mixture was refluxed for 18 h, cooled, and filtered. The solvent and excess $CH_2Cl_2$ were removed under reduced pressure. The residue was thoroughly washed with methanol and recrystallized from THF–MeOH. Pure **11a** (0.846 g) was obtined in 20% yield. **11a**: Mp 270—271 °C; IR (Nujol) 1600 (C=N), 1120, 1005 ($OCH_2O$), 870, 795, 690 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=2.04 (18H, s, $-CH_3$), 5.74 (6H, s, $-CH_2-$); $^{13}C$ NMR ($CDCl_3$) $\delta$=10.57 ($-CH_3$), 99.46 ($-CH_2-$), 155.64 (-C=N-), mass spectrum *m/z* 384 ($M^+$). Found: C, 47.07; H, 6.31; N, 22.15%. Calcd for $C_{15}H_{24}N_6O_6$: C, 46.87; H, 6.29; N, 21.87%.

*3,4,10,11,17,18-Hexaisopropyl-1,6,8,13,15,20-hexaoxa-2,5,9,12,16,19-hexaazahenicosa-2,4,9,11,16,18-hexaene (**11b**).* The reaction of (*E,E*)-2,5-dimethyl-3,4-hexanedione dioxime **10b** (0.152 g, 0.88 mmol) with $Bu^tOK$ (0.199 g, 1.77 mmol) and 18-crown-6 (0.023 g, 0.088 mmol) in THF (6 mL) and $CH_2Cl_2$ (6 mL) gave **11b** (0.033 g, 21%) which was purified by preparative TLC ($SiO_2$, ethyl acetate:hexane=1:10). **11b**: Mp 140—148 °C; IR (Nujol) 1595 (C=N), 1060, 1030 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.14 (36H, d, *J*=7 Hz, $-CH_3$), 3.33 (6H, heptet, *J*=7 Hz, -CH), 5.63 (6H, s, $-CH_2-$); mass spectrum *m/z* 551 ($M^+-1$).

*3,4,10,11,17,18,24,25-Octapropyl-1,6,8,13,15,20,22,27-octaoxa-2,5,9,12,16,19,23,26-octaazaoctacosa-2,4,9,11,16,18,23,25-octaene (**12**).* This compound was prepared by the reaction of (*E,E*)-4,5-octanedione dioxime **10c** (1.033 g, 6 mmol) with $Bu^tOK$ (1.346 g, 12 mmol) and 18-crown-6 (0.159 g, 0.6 mmol) in THF (20 mL) and $CH_2Cl_2$ (20 mL). The product (40% yield) was isolated by preparative TLC ($SiO_2$, ethyl acetate: hexane=1:15). Analytically pure sample was obtained by two additional preparative TLC. **12**: Mp 143—146 °C; IR (Nujol) 1595 (C=N), 1135, 1020 ($OCH_2O$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=0.84 (24H, t, *J*=7 Hz, $-CH_3$), 1.14—1.73 (16H, m, $-CH_2-$), 2.63 (16H, t, *J*=7 Hz, $-CH_2C$=N-), 5.70 (8H, s, $-OCH_2O-$); $^{13}C$ NMR ($CDCl_3$) $\delta$=14.13 ($-CH_3$), 19.93 ($-CH_2-$), 26.12 ($-CH_2-$), 99.32 ($-OCH_2O-$), 158.32 (-C=N-), mass spectrum *m/z* 736 ($M^+$). Found: C, 58.58; H, 8.70; N, 15.29%. Calcd for $C_{36}H_{64}N_8O_8$: C, 58.67; H, 8.75; N, 15.21%.

*7H-3,4-Dicyclohexyl-1,6,2,5-dioxadiazepine (**15a**).* This compound was prepared by the reaction of (*Z,Z*)-dicyclohexylethanedione dioxime **10f** (1.001 g, 4 mmol) with $Bu^tOK$ (0.898 g, 8 mmol) and 18-crown-6 (0.106 g, 0.4 mmol) in

THF (20 mL) and $CH_2Cl_2$ (20 mL). The product (66% yield) was purified by preparative TLC ($SiO_2$, ethyl acetate:hexane=1:15). **15a**: Bp 135—136 °C/1 mmHg; IR (neat) 1600 (C=N), 1035 ($OCH_2O$), 990, 975 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 0.98—2.58 (22H, m, $-CH_2-$), 5.28 (2H, s, $-OCH_2O-$); mass spectrum *m/z* 265 ($M^+$+1). Found: C, 67.79; H, 9.13, N, 10.42%. Calcd for $C_{15}H_{24}N_2O_2$: C, 68.15; H, 9.15; N, 10.60%.

*Reaction of (Z,Z)-2,5-Dimethyl-3,4-hexanedione Dioxime* ***10g*** *with Dichloromethane.* In a 100 mL flask containing a Teflon-coated magnetic stirrer bar were placed (*Z,Z*)-2,5-dimethyl-3,4-hexanedione dioxime **10g** (1.033 g, 6 mmol), Bu$^t$OK (1.346 g, 12 mmol) and 18-crown-6 (0.159 g, 0.6 mmol). Into the flask was added $CH_2Cl_2$ (20 mL) with stirring, and then THF (20 mL) was slowly added to the resulting suspended solution in an ice bath. After the addition was complete, the mixture was refluxed for 20 h. cooled, and filtered. After removal of THF and $CH_2Cl_2$ under reduced pressure, the products were chromatographed on $Al_2O_3$. A mixture of **15b** and **16** obtained from the elution of ether was purified by preparative TLC ($SiO_2$, ethyl acetate:hexane=1:10). Pure **15b** (0.517 g) and **16** (0.044 g) were obtained in 47% and 4% yield, respectively. **15b**: Bp 60—61 °C/1 mmHg; IR (neat) 1605 (C=N), 1035 ($OCH_2O$), 975 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.25 (12H, d, *J*= 7 Hz, $-CH_3$), 2.68 (2H, heptet, *J*=7 Hz, >CH), 5.30 (2H, s, $-CH_2-$); mass spectrum *m/z* 184 ($M^+$). Found: C, 58.61; H, 8.57; N, 15.26%. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21%. **16**: Mp 82—83 °C; IR (Nujol) 1615 (C=N), 1260, 1020 ($OCH_2O$); $^1H$ NMR ($CDCl_3$) $\delta$=1.14 (12H, d, *J*= 7 Hz, $-CH_3$), 1.19 (12H, d, *J*=7 Hz, $-CH_3$), 2.60 (4H, m, -CH), 5.55 (4H, s, $-CH_2-$); mass spectrum *m/z* 368 ($M^+$). Found: C, 58.99; H, 8.61; N, 14.87. Calcd for $C_{18}H_{32}N_4O_4$: C, 58.66; H, 8.75; N, 15.21.

*Reaction of (Z,E)-2,5-Dimethyl-3,4-hexanedione Dioxime* ***10h*** *with Dichloromethane.* In a 50 mL flask containing a Teflon-coated magnetic stirrer bar were placed (*Z,E*)-2,5-dimethyl-3,4-hexanedione dioxime **10h** (0.360 g, 2.1 mmol), Bu$^t$OK (0.471 g, 4.2 mmol) and 18-crown-6 (0.055 g, 0.21 mmol). Into the flask was added $CH_2Cl_2$ (10 mL) with stirring, and then THF (10 mL) was slowly added to the resulting suspended solution in an ice bath. After the addition was complete, the mixture was refluxed for 20 h, cooled, and filtered. After removal of THF and $CH_2Cl_2$ under reduced pressure, the residue was purified by preparative TLC ($R_f$ 0.70, $SiO_2$, ethyl acetate:hexane=3:7) to give **15b** (0.043 g, 16%).

*Reaction of (E,E)-1,2-Cyclohexanedione Dioxime* ***10e*** *with Dichloromethane.* The reaction of (*E,E*)-1,2-cyclohexanedione dioxime **10e** (0.976 g, 6.8 mmol), Bu$^t$OK (1.526 g, 13.6 mmol) and 18-crown-6 (0.186 g, 0.68 mmol) in $CH_2Cl_2$ (80 mL) gave **13** (0.112 g, 12%) which was purified by silica-gel column chromatography (ether as eluting solvent). **13**: Mp 178—180 °C; IR (Nujol) 3200 (OH), 1620 (C=N), 1140, 1015 ($OCH_2O$), 820, 765 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.43—1.93 (8H, m, $-CH_2-$) 2.45—2.95 (8H, m, $-CH_2-$), 4.20—5.30 (2H, br, -OH), 5.85 (2H, s, $-OCH_2O-$). Found: C, 52.62; H, 6.66; N, 18.65%. Calcd for $C_{13}H_{20}N_4O_4$: C, 52.69; H, 6.80; N, 18.91%.

*Reaction of (E,E)-Benzil Dioxime* ***10d*** *with Dichloromethane.* The reaction of (*E,E*)-benzil dioxime **10d** (0.961 g, 4 mmol), Bu$^t$OK (0.896 g, 8 mmol) and 18-crown-6 (0.106 g, 0.4 mmol) in $CH_2Cl_2$ (40 mL) gave 3,4-diphenylfrazan **14** (0.236 g, 27%) which was purified by $Al_2O_3$ column chromatography (pentane:ether=9:1). **14**: Mp 91—92 °C; IR (Nujol) 1580 (C=N), 1075, 990, 890, 780, 760, 695 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$= 7.25—7.68 (10H, m, aromatic). Found: C, 75.75; H, 4.49; N, 12.76%. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.61%.

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