

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

Takahiho HOSOKAWA,* Toshiyuki OHTA, Yoshihiro OKAMOTO, and Shun-Ichi MURAHASHI*

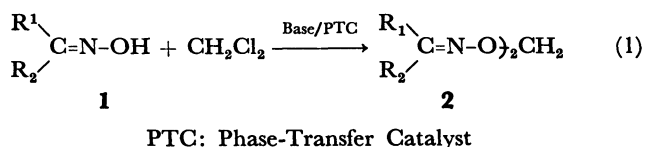
Department of Chemistry, Faculty of Engineering Science, Osaka University,
Machikaneyama, Toyonaka, Osaka 560

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Ketoximes, when treated with KO_2 (1 equiv) in the presence of di- μ -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 heteromacrocylic compounds in which oxime units are sequentially linked by methylene bridge.

Previously we have reported palladium-induced deoxygenation¹⁾ and Beckmann fragmentation of ketoximes²⁾ by the use of peroxobis(triphenylphosphine)palladium(II), $(\text{PPh}_3)_2\text{Pd} \begin{smallmatrix} \text{O} \\ \diagup \quad \diagdown \\ | \end{smallmatrix}$. 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,



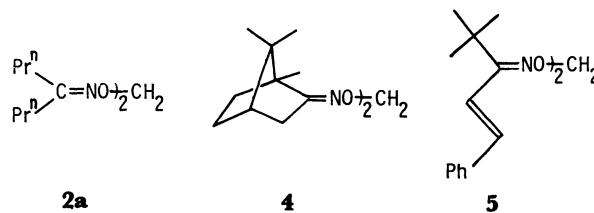
interestingly, these two systems have shown an inverse reactivity toward aryl and alkyl ketoximes.

Application of the reaction to 1,2-diketone dioximes, *e.g.*, dimethylglyoxime, has led to the synthesis of a novel heteromacrocylic compound formed *via* a sequential oligomerization of the dioxime and dichloromethane. Although a variety of macrocylic polyether and azacrown compounds have been reported in literatures,⁵⁾ there are few examples of heteromacrocylics containing oxime linkages. These are Vögtle's macrocylic mono- and dioximes⁶⁾ prepared from 1,2-diketone dioximes and 1, ω -dichloro-oligo-1-oxapropene $[\text{Cl}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{Cl}]$ ⁷⁾ and Sarlo's macrocylic 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

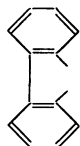
Reaction of Ketoximes with CH_2Cl_2 In the present study, ketoximes (**1**) have been generally allowed to react with an equimolar amount of KO_2 in dichloromethane in the presence of $[(2\text{-methylallyl})\text{PdCl}]_2$ (**3**) (0.1 equiv per Pd). Under the conditions, a relatively wide range of 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



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 $\text{PdCl}_2-(\text{CH}_3\text{CN})_2$ and $\text{Pd}(\text{OAc})_2$ 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 ₂ CO ₃ /18-c-6 ^{b)}	KO ₂ /18-c-6 ^{b)}	Bu ^t OK/18-c-6 ^{b)}
1	C ₃ H ₇	C ₃ H 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 ₂ CH ₂	PhCH ₂ CH 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 (<i>E</i>)	(1h)	0	92		

a) Isolated yield. b) In this system, yields were determined by ¹H NMR spectroscopy. c) Isolated yield when 2 equiv of KO₂ was used.

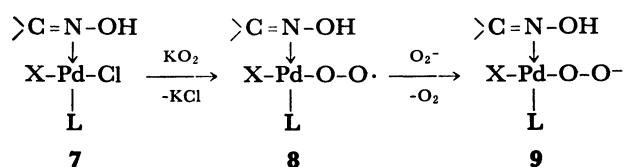
These results prompted us to examine the difference in reactivity between the two reaction systems using a series of ketoximes. From Table 1, it can be seen that in the former system aliphatic ketoximes afford higher yields of methylene dioxime than aryl ketoximes, whereas the opposite trend is observed in the latter (K₂CO₃/18-c-6). Further, the reactivities observed in both systems appear to change as a function of the pK_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 K₂CO₃ was replaced with more basic Bu^tOK, the aliphatic ketoxime **1b** gives methylene dioxime **2b** in a good yield (74%). The use of KO₂ with 18-crown-6 gives **2b** only in 27% yield in accordance with the order of decrease in basicity (Bu^tOK > KO₂ > K₂CO₃).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 KO₂ acts as a Brønsted base in the presence of phase-transfer agents.¹²⁾

In the KO₂-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 [(R₂C=NO)₂(R₂C=NOH)₂]Pd (**6**) by comparing the spectra data with those of the authentic complex **6a** (R = CH₂Ph) prepared from Pd(acac)₂ and dibenzyl ketone oxime.¹³⁾ Thus, when the oxime has lower pK_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 successive, nucleophilic displace-

ment of an oximate anion to dichloromethane. In the former system (KO₂/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 (O₂^{•-}) is then transferred into the organic phase *via* anion exchange (**7**→**8**) with the chloride ligand of Pd(II) complex. Electron transfer (**8**→**9**) followed by proton abstraction¹⁴⁾ results in the formation of oximate anion in the coordination sphere of palladium(II). Alternatively, the oximate anion may be

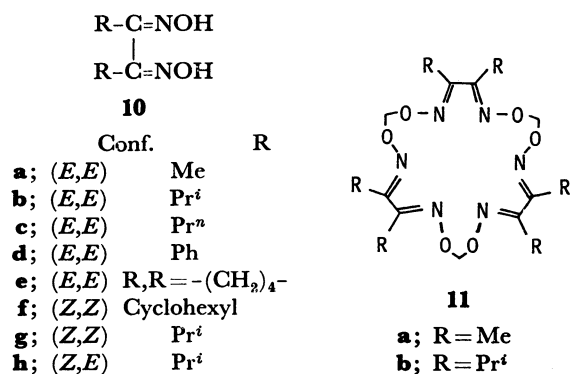


directly formed from the coordinated oxime **7** by the action of KO₂ with releasing HOO[•]. In any case, depending on its nucleophilicity, the oximate anion thus produced attacks at the methylene carbon of CH₂Cl₂.¹⁵⁾ Since less acidic ketoximes readily undergo the reaction in this system, the acidity of oximes must be enhanced by its coordination to palladium(II).

Reaction of 1,2-Diketone Dioxime with CH₂Cl₂.

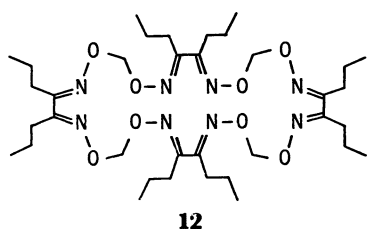
Application of the present methods to 1,2-diketone dioximes (**10**) resulted in either formation of nitractable palladium complexes (KO₂/Pd(II)) or recovery of the starting materials (K₂CO₃/18-c-6). However, the use of Bu^tOK in the presence of 18-crown-6 led to a successful synthesis of novel dioxime 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^tOK (2 equiv) and 18-crown-6 (0.1 equiv) in THF was slowly added an excess of dichloromethane, and the mixture



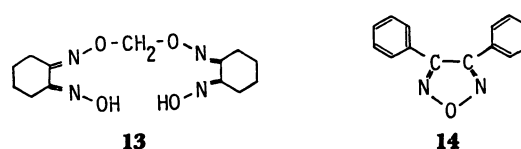
was refluxed. After filtration of the reaction mixture and evaporation of the solvent and excess CH₂Cl₂, the residue was thoroughly washed with methanol to remove unreacted oxime **10a**. The remaining solid was recrystallized from MeOH-THF to give **11a** in 20% yield as colorless crystals. In the absence 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 CH₂Cl₂.

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



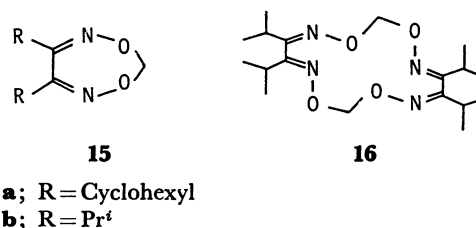
In the ¹H NMR spectra of **11a**, **11b**, and **12**, the -OCH₂O- protons appear as a singlet approximately at δ 5.50, and their ¹³C{¹H} NMR spectra (CDCl₃) also exhibit only singlet due to the methylene carbon at δ 99.45 ppm for **11a** and δ 99.31 ppm for **12** relative to Me₄Si. These results indicate the equivalence of all the -OCH₂O- groups. In addition, the signal of alkyl substituent (R=Me, Prⁱ, and Prⁿ) 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=-(CH₂)₄-) and **10d** (R=Ph). Thus, (*E,E*)-1,2-cyclohexanedione dioxime (**10e**) gave



a 12% yield of **13**, a 2:1 adduct of the dioxime and CH₂Cl₂. (*E,E*)-benzil dioxime **10d** gave a 27% yield of 3,4-diphenylfurazan **14** formally *via* (*E,E*) ⇌ (*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 CH₂Cl₂ 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



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 ¹H NMR spectrum.

The (*Z,E*)-dioxime **10h** (R=Prⁱ) also gave the dioxadiazepine **15b** in 16% yield, but the expected product **16** was not formed. In any case, when the substituent is Prⁱ, (*Z,E*) ⇌ (*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 (δ) expressed in parts per million relative to Me₄Si. 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-μ-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 solution 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-hexanedione²⁰ (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 monoxime (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) δ=0.73 (12H, d, *J*=7 Hz, -CH₃), 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 (SiO₂, 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) δ=1.05 (12H, d, *J*=7 Hz, -CH₃), 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) δ=0.99 (d, *J*=7 Hz, -CH₃, 6H), 1.03 (d, *J*=7 Hz, -CH₃, 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-octanedione²⁰ 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) δ=0.70 (6H, m, -CH₃), 1.00–1.60 (4H, m, -CH₂-), 2.38 (4H, m, -C(=N)-CH₂-), 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-dicyclohexylethanedione²⁰ 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) δ=0.91–2.46 (20H, m, -CH₂-), 10.28 (2H, s, -OH). The configura-

tion assignment of the dioxime was made similarly as above.

Reaction of Ketoximes with Dichloromethane in the Presence of KO₂ 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- μ -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 Al₂O₃ 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 analytical 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 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=0.92 (12H, t, *J*=7 Hz, -CH₃), 1.48 (8H, m, -CH₂-), 2.13 (8H, q, *J*=7 Hz, -CH₂C=N-), 5.37 (2H, s, -OCH₂O-). Found: C, 66.58; H, 11.38; N, 10.36%. Calcd for C₁₅H₃₀N₂O₂: C, 66.62; H, 11.18; N, 10.10%.

Methylene Dioxime 2b: Mp 39 °C; IR (Nujol) 1640 (C=N), 1150, 1020 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=1.80 (12H, s, -CH₃), 5.30 (2H, s, -CH₂-). Found: C, 53.04; H, 8.92; N, 17.85%. Calcd for C₇H₁₄N₂O₂: C, 53.14; H, 8.91; N, 17.71%.

Methylene Dioxime 2c: Mp 47–48.5 °C; IR (Nujol) 1645 (C=N), 1135, 1020 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=1.60 (12H, m, -CH₂-), 2.18 (4H, m, -CH₂-), 2.47 (4H, m, -CH₂-), 5.37 (2H, s, -OCH₂O-). Found: C, 65.75; H, 9.41; N, 11.49%. Calcd for C₁₃H₂₂N₂O₂: C, 65.51; H, 9.31; N, 11.76%.

Methylene Dioxime 2d: Mp 73 °C; IR (Nujol) 1628 (C=N), 1150, 1028 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=2.20–3.03 (16H, m, -CH₂-), 5.71 (2H, s, -OCH₂O-), 7.03–7.40 (20H, m, aromatic). Found: C, 81.27; H, 7.38; N, 5.42%. Calcd for C₃₅H₃₈N₂O₂: C, 81.04; H, 7.38; N, 5.40%.

Methylene Dioxime 2e: Mp 102 °C; IR (Nujol) 1630 (C=N), 1148, 1024 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=3.43 (4H, s, -CH₂-), 3.63 (4H, s, -CH₂-), 5.80 (2H, s, -OCH₂O-), 7.00–7.27 (20H, m, aromatic). Found: C, 80.71; H, 6.55; N, 6.10%. Calcd for C₃₁H₃₀N₂O₂: C, 80.49; H, 6.54; N, 6.06%.

Methylene Dioxime 2f: Mp 90–91 °C; IR (Nujol) 1150, 1020 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=5.70 (2H, s, -CH₂-), 7.10–7.60 (20H, m, aromatic). Found: C, 79.99; H, 5.32; N, 6.79%. Calcd for C₂₇H₁₈N₂O₂: C, 79.78; H, 5.46; N, 6.89%.

Methylene Dioxime 2g: Mp 211–211.5 °C; IR (Nujol) 1620 (C=N), 1021 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=6.20 (2H, s, -CH₂-), 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 C₂₇H₂₂N₂O₂: 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 (OCH₂O) cm⁻¹; ¹H NMR (CCl₄) δ=5.76 (2H, s, -CH₂-), 7.03–8.03 (20H, m, aromatic). Found: C, 75.40; H, 4.72; N, 6.16%. Calcd for C₂₆H₂₂N₂O₄: C, 75.31; H, 4.79; N, 6.06%.

Methylene Dioxime 4: Yield 32%; mp 68 °C; IR (Nujol) 1675 (=N), 1005 (OCH₂O) cm⁻¹; ¹H NMR (CDCl₃) δ=0.77 (6H, s, -CH₃), 0.90 (6H, s, -CH₃), 1.00 (6H, s, -CH₃),

1.07–2.73 (14H, m, $-\text{CH}_2-$, and $>\text{CH}$), 5.38 (2H, s, $-\text{OCH}_2\text{O}-$). Found: C, 72.50; H, 9.83; N, 7.82%. Calcd for $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_2$: C, 72.79; H, 9.89; N, 8.09%.

Methylene Dioxime 5: Yield 23%; bp 185 °C/0.15 mmHg; IR (neat) 1615 ($\text{C}=\text{N}$), 1245, 1075 cm^{-1} ; ^1H NMR (CDCl_3) δ =1.36 (18H, s, $-\text{Bu}'$), 6.30 (2H, s, $-\text{CH}_2-$), 7.15–7.48 (10H, m, $=\text{CH}-$ and aromatic), 7.58–7.80 (4H, m, $=\text{CH}-$ and aromatic).

The use of $\text{Pd}(\text{OAc})_2$ or $\text{PdCl}_2(\text{PhCN})_2$ in place of [(2-methylallyl) PdCl] $_2$ (**3**) in the reaction of **1b** ($\text{R}=\text{CH}_3$) under the conditions described above also gave the methylene dioxime **2b**. The isolable yield of **2b** were 42% with $\text{Pd}(\text{OAc})_2$ and 34% with $\text{PdCl}_2(\text{PhCN})_2$. 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- μ -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** ($\text{R}=\text{CH}_2\text{Ph}$), (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) δ =2.83–4.13 (16H, m, $-\text{CH}_2-$), 6.77–7.03 (40H, m, aromatic). Found: C, 71.68; H, 5.72; N, 5.63%. Calcd for $\text{C}_{60}\text{H}_{58}\text{N}_4\text{O}_4\text{Pd}$: C, 71.68; H, 5.81; N, 5.57%.

The same reaction with **1d** (0.506 g, 2 mmol) gave the oximate complex **6b** ($\text{R}=\text{CH}_2\text{CH}_2\text{Ph}$), (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) δ =2.75 (32H, m, $-\text{CH}_2-$), 7.00–7.37 (40H, m, aromatic). Found: C, 73.07; H, 6.67; N, 5.06%. Calcd for $\text{C}_{68}\text{H}_{74}\text{N}_4\text{O}_4\text{Pd}$: 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 ($\text{R}=\text{CH}_2\text{Ph}$). A solution of $\text{Pd}(\text{acac})_2$ (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 described 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-hexaazahenicoso-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), $\text{Bu}'\text{OK}$ (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 obtained in 20% yield. **11a**: Mp 270–271 °C; IR (Nujol) 1600 ($\text{C}=\text{N}$), 1120, 1005 (OCH_2O), 870, 795, 690 cm^{-1} ; ^1H NMR (CDCl_3) δ =2.04 (18H, s, $-\text{CH}_3$), 5.74 (6H, s, $-\text{CH}_2-$); ^{13}C NMR (CDCl_3) δ =10.57 ($-\text{CH}_3$), 99.46 ($-\text{CH}_2-$), 155.64 ($-\text{C}=\text{N}-$), mass spectrum m/z 384 (M^+). Found: C, 47.07; H, 6.31; N, 22.15%. Calcd for $\text{C}_{15}\text{H}_{24}\text{N}_6\text{O}_6$: 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-hexaazahenicoso-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 $\text{Bu}'\text{OK}$ (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 ($\text{C}=\text{N}$), 1060, 1030 cm^{-1} ; ^1H NMR (CDCl_3) δ =1.14 (36H, d, $J=7$ Hz, $-\text{CH}_3$), 3.33 (6H, heptet, $J=7$ Hz, $-\text{CH}$), 5.63 (6H, s, $-\text{CH}_2-$); 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-octaazaoctacosso-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 $\text{Bu}'\text{OK}$ (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 ($\text{C}=\text{N}$), 1135, 1020 (OCH_2O) cm^{-1} ; ^1H NMR (CDCl_3) δ =0.84 (24H, t, $J=7$ Hz, $-\text{CH}_3$), 1.14–1.73 (16H, m, $-\text{CH}_2-$), 2.63 (16H, t, $J=7$ Hz, $-\text{CH}_2\text{C}=\text{N}-$), 5.70 (8H, s, $-\text{OCH}_2\text{O}-$); ^{13}C NMR (CDCl_3) δ =14.13 ($-\text{CH}_3$), 19.93 ($-\text{CH}_2-$), 26.12 ($-\text{CH}_2-$), 99.32 ($-\text{OCH}_2\text{O}-$), 158.32 ($-\text{C}=\text{N}-$), mass spectrum m/z 736 (M^+). Found: C, 58.58; H, 8.70; N, 15.29%. Calcd for $\text{C}_{36}\text{H}_{64}\text{N}_8\text{O}_8$: 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 $\text{Bu}'\text{OK}$ (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 ($\text{C}=\text{N}$), 1035 (OCH_2O), 990, 975 cm^{-1} ; ^1H NMR (CDCl_3) δ =0.98–2.58 (22H, m, $-\text{CH}_2-$), 5.28 (2H, s, $-\text{OCH}_2\text{O}-$); mass spectrum m/z 265 (M^++1). Found: C, 67.79; H, 9.13, N, 10.42%. Calcd for $\text{C}_{15}\text{H}_{24}\text{N}_2\text{O}_2$: 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^tOK (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 ($\text{C}=\text{N}$), 1035 (OCH_2O), 975 cm^{-1} ; ^1H NMR (CDCl_3) δ =1.25 (12H, d, J =7 Hz, $-\text{CH}_3$), 2.68 (2H, heptet, J =7 Hz, $>\text{CH}$), 5.30 (2H, s, $-\text{CH}_2-$); mass spectrum m/z 184 (M^+). Found: C, 58.61; H, 8.57; N, 15.26%. Calcd for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2$: C, 58.67; H, 8.75; N, 15.21%. **16**: Mp 82–83 °C; IR (Nujol) 1615 ($\text{C}=\text{N}$), 1260, 1020 (OCH_2O); ^1H NMR (CDCl_3) δ =1.14 (12H, d, J =7 Hz, $-\text{CH}_3$), 1.19 (12H, d, J =7 Hz, $-\text{CH}_3$), 2.60 (4H, m, $-\text{CH}$), 5.55 (4H, s, $-\text{CH}_2-$); mass spectrum m/z 368 (M^+). Found: C, 58.99; H, 8.61; N, 14.87. Calcd for $\text{C}_{18}\text{H}_{32}\text{N}_4\text{O}_4$: 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^tOK (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^tOK (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 ($\text{C}=\text{N}$), 1140, 1015 (OCH_2O), 820, 765 cm^{-1} ; ^1H NMR (CDCl_3) δ =1.43–1.93 (8H, m, $-\text{CH}_2-$), 2.45–2.95 (8H, m, $-\text{CH}_2-$), 4.20–5.30 (2H, br, $-\text{OH}$), 5.85 (2H, s, $-\text{OCH}_2\text{O}-$). Found: C, 52.62; H, 6.66; N, 18.65%. Calcd for $\text{C}_{13}\text{H}_{20}\text{N}_4\text{O}_4$: 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^tOK (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 ($\text{C}=\text{N}$), 1075, 990, 890, 780, 760, 695 cm^{-1} ; ^1H NMR (CCl_4) δ =7.25–7.68 (10H, m, aromatic). Found: C, 75.75; H, 4.49; N, 12.76%. Calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}$: C, 75.66; H, 4.54; N, 12.61%.

References

- 1) K. Maeda, I. Moritani, T. Hosokawa, and S-I. Murahashi, *Tetrahedron Lett.*, **1974**, 797.
- 2) K. Maeda, I. Moritani, T. Hosokawa, and S-I. Murahashi, *J. Chem. Soc., Chem. Commun.*, **1975**, 689.
- 3) As a preliminary report, see; T. Hosokawa, T. Ohta, Y. Okamoto, S-I. Murahashi, *Tetrahedron Lett.*, **1980**, 1259. Synthesis of the same compound by similar methods has been independently reported by S. J. Kirsch and H. Schellig, *J. Org. Chem.*, **44**, 3970 (1979), and H. Shinozaki, N. Yoshida, and M. Tajima, *Chem. Lett.*, **1980**, 869.
- 4) K. Holmberg and B. Hansen, *Tetrahedron Lett.*, **1975**, 2303.
- 5) a) J. S. Bradshaw and P. E. Stott, *Tetrahedron*, **36**, 461 (1980); b) G. W. Gokel, D. M. Dishong, R. A. Shultz, and V. J. Gatto, *Synthesis*, **1982**, 997.
- 6) W. Rasshofer, W. M. Müller, G. Oepen, and F. Vögtle, *J. Chem. Res.*, (S), 72; (M), 1001 (1978).
- 7) a) C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967); b) J. S. Bradshaw, "Synthetic Multidentate Macrocyclic Compounds," ed by R. M. Izatt and J. J. Christensen, Academic Press, New York, 1978.
- 8) a) A. Brandi, F. D. Sarlo, and A. Guarna, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 1827; b) F. D. Sarlo, A. Guarna, and G. P. Speroni, *J. Chem. Soc., Chem. Commun.*, **1977**, 549.
- 9) A similar trend of reactivity has been observed in the reaction of arylhydrazine and hydrazone with KO_2 ; see, C-I. Chern and J. S. Filippo, Jr., *J. Org. Chem.*, **42**, 178 (1977).
- 10) M. Fedorynski, K. Wojciechowski, Z. Matacz, and M. Makosza, *J. Org. Chem.*, **43**, 4682 (1978).
- 11) A. A. Frimer, G. Aljadeff, and J. Ziv, *J. Org. Chem.*, **48**, 1700 (1983).
- 12) a) E. Lee-Ruff, *Chem. Soc. Rev.*, **6**, 195 (1977); b) D. T. Sawyer, *Acc. Chem. Res.*, **13**, 105 (1979); c) D. T. Sawyer and M. J. Gibian, *Tetrahedron*, **35**, 1471 (1979); d) J. S. Valentine, "Biochemical and Clinical Aspects of Oxygen," ed by W. S. Caughey, Academic Press, New York (1979), pp. 659–677; e) D. T. Sawyer and J. S. Valentine, *Acc. Chem. Res.*, **14**, 393 (1981).
- 13) S. Imamura, T. Kajimoto, Y. Kitano and J. Tsuji, *Bull. Chem. Soc. Jpn.*, **42**, 805 (1969).
- 14) a) H. Suzuki, K. Mizutani, Y. Moro-oka, and T. Ikawa, *J. Am. Chem. Soc.*, **101**, 748 (1979); b) F. Sakurai, H. Suzuki, Y. Moro-oka, and T. Ikawa, *ibid.*, **102**, 1749 (1980); c) Y. Moro-oka and H. Suzuki, *J. Syn. Org. Chem. Jpn.*, **41**, 316 (1983).
- 15) It has been reported that the reaction of π -allyl palladium(II) complex **3** with KO_2 in CH_2Cl_2 gives μ -peroxobis(2-methylallyl)dipalladium(II) which behaves as a relatively stronger base.¹⁴ However, this type of the complex is not involved in the present reaction, because when the complex was treated with dibenzyl ketone oxime in CH_2Cl_2 , no methylene dioxime was formed. The only isolable product in this experiment was a trace or negligible amount of dibenzyl ketone. Although in one run the yield was 20%, its reproducibility was found to be poor in further runs.

- 16) W. T. Dent, R. Long, and A. J. Wilkinson, *J. Chem. Soc.*, **1964**, 1585.
- 17) T. Hosokawa, S. Miyagi, S-I. Murahashi, and A. Sonoda, *J. Org. Chem.*, **43**, 2752 (1978).
- 18) J. R. Doyle, P. E. Slade, and H. B. Jonassen, *Inorg. Synth.*, **6**, 218 (1960).
- 19) T. W. J. Taylor and M. S. Marks, *J. Chem. Soc.*, **1930**, 2302.
- 20) The 1,2-diketone was prepared by a similar method reported by Y. Ogata and M. Yamashita, *Tetrahedron*, **27**, 3395 (1971).
- 21) M. Tanaka, T. Shono, and K. Shinra, *Anal. Chim. Acta.*, **46**, 125 (1969).
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