# Syntheses of O-Methylated-1,2,4-dioxazolidines by Ozonolyses of O-Methylated Dioximes

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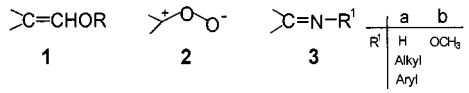
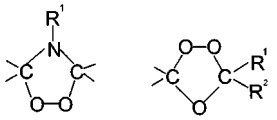
It has been reported that ozonolyses of a variety of vinyl ethers **1** in the presence of a number of imines **3a** afforded the corresponding monocyclic 1,2,4-dioxazolidines **4** by [3+2] cycloaddition of the carbonyl oxides **2** derived from **1** and the C=N moieties in the imines **3a**.[1,2]




1 2 3

O-Methylated oximes **3b** are also cleaved by ozone to give carbonyl oxides **2**.[3] Ozonolyses of O-methylated oximes **3b** in the presence of acid derivatives or carbonyl compounds $R^1COR^2$ to give the corresponding cross-ozonides **5** have been reported.[4,5]

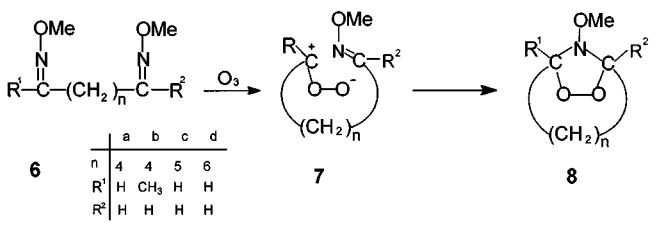


4 5

On the basis of the above results, monoozonolyses of O-methylated dioximes of dicarbonyl compounds in the absence of added carbonyl compounds would be expected to give the corresponding bicyclic dioxazolidines. Recently, K. Griesbaum[6] has made use of this by ozonizing O-methylated dioximes of type **6** with $n = 2$ and $n = 3$ to prepared the corresponding 1,2,4-dioxazolidines.

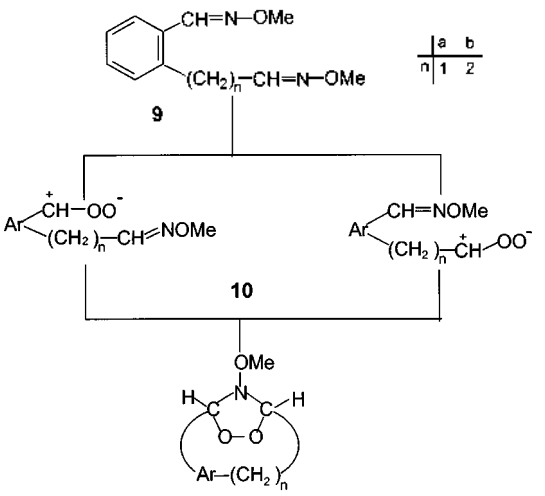
Extending these studies, we have now ozonized the acyclic O-methylated dioximes **6a-6d** with $n = 4$ to $n = 6$ and the aromatic O-methylated dioximes **9a** and **9b**. Ozonolyses of **6a-d** in dichloromethane at -78 °C afforded the corresponding bicyclic 1,2,4-dioxazolidines **8a-d** in yields of 67 %, 59%, 31% and 53%, respectively. These results show that intramolecular trapping of the carbonyl oxide moiety with the C=N bond of intermediate **7** can be effectively performed as outlined in Scheme 1.

Ozonolyses of the aromatic O-methylated dioximes **9a**




6 7 8

Scheme 1



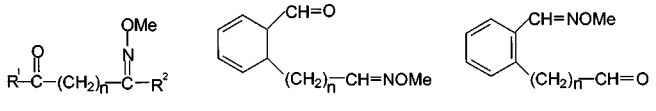

9 10 11

Scheme 2

and **9b** in dichloromethane at -78 °C afforded the corresponding aromatic 1,2,4-dioxazolidines **11a** and **11b** *via* intermediates **10** in yields of 65% and 35%, respectively (Scheme 2).

All of the 1,2,4-dioxazolidines **8** and **11** have been isolated by column chromatography on silica gel and their structures were established by $^1H$ and $^{13}C$ NMR spectroscopy. Characteristic signals in the $^1H$ NMR spectra of all 1,2,4-dioxazolidines of type **8** and **11** were those for the $OCH_3$ and $CH_2$ groups. The $OCH_3$ groups showed singlet signals in the range of $\delta = 3.48$-$3.81$ and the $CH_2$ groups showed singlet signals in the range of $\delta = 5.29$-$6.00$. Characteristic signals in the $^{13}C$ NMR spectra of all dioxazolidines of type **8** and **11** were those for the $OCH_3$-carbon atoms and the carbon atoms in the heterocyclic rings. The signals for the $OCH_3$-carbon atoms appeared in the range of $\delta = 61.05$-$62.56$ and those for the carbon atom in the heterocyclic rings appeared in the range of $\delta = 94.67$-$103.91$.

Reductions of **8a-d** with TPP gave the corresponding monooximes **12**, whereas reductions of **11a** and **11b** afforded both of the two possible monooximes **13** and **14**. Reduction of **11a** gave **13a** and **14a** in a ratio of *ca.* 1 : 1 and **11b** gave **13b** and **14b** in a ratio of *ca.* 7 : 1.




12 13 14

## Experimental Section

All **NMR** spectra were recored with Bruker **FT-NMR** (300 MHz), using **TMS** as internal reference. The ozonides were isolated by flash chromatography on 80 g silica gel using diethyl ether/*n*-pentane in a ratio of 1 : 2.

Substrates **6a-d** and **9a-b** were prepared according to a published procedure[7] by reactions of the corresponding dicarbonyl compounds with an excess of O-methyl hydroxylamine hydrochloride, and isolated by flash chromatography. As shown by $^1$H NMR analysis **6a-d** were obtained as mixtures of isomers: **6a** $^1$H NMR: $\delta$ 1.51 (m, 4H), [2.19 (m) 2.35 (m)](4H), [3.81 (s), 3.85 (s)](6H), [6.65 (t), 7.32 (t)](2H). $^{13}$C NMR: $\delta$ 24.45, 25.51, 25.97, 26.43, 29.42, 33.91, 61.49, 61.85, 150.50, 151.41.]; **6b** $^1$H NMR: $\delta$ 1.52 (m, 4H), [1.81 (s), 1.83 (s)](3H), 2.23 (m, 4H), [3.79 (s), 3.82 (s)](6H), [6.62 (t), 7.35 (t)](1H). $^{13}$C NMR: $\delta$ 14.15, 25.63-26.58 (m), 29.55, 35.84, 61.47, 61.56, 61.92, 150.81, 151.73, 157.63.; **6c** $^1$H NMR: $\delta$ 1.32-1.56 (m, 6H), [2.15 (m), 2.32 (m)](4H), [3.74 (s), 3.85 (s)](6H), [6.60 (t), 7.32 (t)](2H). $^{13}$C NMR: $\delta$ 26.70, 29.06, 29.59, 61.47, 61.84, 150.84, 151.77; **6d** $^1$H NMR: $\delta$ 1.52 (m, 4H), 1.81 (m, 4H), [2.23 (m), 2.35 (m)](4H), [3.79 (s), 3.82 (s)](6H), [6.62 (t), 7.35 (t)](2H). $^{13}$C NMR: $\delta$ 24.93, 25.12, 26.89, 29.05, 29.25, 29.69, 61.47, 61.84, 151.09, 152.04; **9a** $^1$H NMR: $\delta$ [3.45 (m), 3.68 (m)](2H), [3.93 (s), 3.98 (s)](3H), [6.68 (t), 7.43 (t)](1H), 7.29-7.67 (m, 4H), [8.24 (s), 8.31 (s)](1H). $^{13}$C NMR: $\delta$ 31.09, 34.46, 62.65, 62.69, 62.90, 127.90, 127.99, 128.12, 131.77, 132.99, 133.00, 135.49, 136.00, 145.07, 145.38, 148.25, 148.31; **9b** $^1$H NMR: $\delta$ 2.77 (m, 2H), 3.10 (m, 2H), [3.83 (s), 3.84 (s)](3H), 4.00 (s, 3H), 7.37 (t, 1H), 7.40-7.90 (m, 4H), 8.54 (s, 1H). $^{13}$C NMR: $\delta$ 27.51, 30.08, 62.09, 62.38, 127.12, 128.09, 130.47, 139.96, 147.62, 150.48.

**General ozonolysis procedure**. A solution of the respective substrates (3.4 mmol) in 50 mL of dichloromethane was treated with ozone at -78 °C until the solution turned blue. Residual ozone was flushed off with nitrogen, the solvent was distilled off at room temperature and reduced pressure, and from the remaining residue, the products **8a-8d** and **11a-11b** were isolated by flash chromatography using silica gel and *n*-pentane/diethyl ether in a ratio of 4 : 1.

**Reduction reactions**. A solution of a dioxazolidine in 1 mL of $CDCl_3$ was admixed with excess TPP in a NMR tube and kept at room temperature until $^1$H NMR analysis showed the disappearance of the substrate.

***N*-Methoxy-7,8,9-dioxazo-bicyclo[4.2.1]nonane (8a)**: Yeild, 67%; colorless liquid; $^1$H NMR: $\delta$ = 1.56-1.82 (m, 8H), 3.63 (s, 3H), 5.47 (t, $J$ = 3.12 Hz, 2H); $^{13}$C NMR: $\delta$ = 22.78, 31.94, 61.69, 100.13. Anal. calcd. for $C_7H_{13}NO_3$ (159.2): C, 52.82; H, 8.23. found: C, 52.77; H, 8.35.

**Reduction of 8a** with TPP gave **12a** as the sole product [$\delta$ 3.82 (s), 7.31 (t), 10.05 (s)].

**1-Methyl-*N*-methoxy-8,9,10-dioxazobicyclo[4.2.1]decane (8b)**: Yeild, 59%; colorless liquid; $^1$H NMR: $\delta$ = 1.53 (s, 3H), 1.54-1.83 (m, 8H), 3.54 (s, 3H), 5.43 (t, $J$ = 3.12 Hz, 1H); $^{13}$C NMR: $\delta$ = 19.96, 22.89, 23.43, 40.23, 62.35, 102.73, 103.47. Anal. calcd. for $C_8H_{15}NO_3$ (173.2): C, 55.48; H, 8.73. found: C, 55.67; H, 8.84.

**Reduction of 8b** with TPP gave **12b** as the sole product [$\delta$ 1.81(s), 3.85 (s), 10.04 (s)].

***N*-Methoxy-8,9,10-dioxazobicyclo[5.2.1]undecane (8c)**: Yeild, 31%; colorless liquid; $^1$H NMR: $\delta$ = 1.25-1.76 (m, 10H), 3.80 (s, 3H), 5.29 (s, 2H); $^{13}$C NMR: $\delta$ = 31.14, 33.53, 34.26, 61.92, 62.56, 100.25. Anal. calcd. for $C_8H_{15}NO_3$ (173.2): C, 55.48; H, 8.73. found: C, 55.76; H, 8.91.

**Reduction of 8c** with TPP gave **12c** as the sole product [$\delta$ 3.85 (s), 7.35 (s), 10.08 (s)].

***N*-Methoxy-9,10,11-dioxazobicyclo[6.2.1]dodecane (8d)**: Yeild, 53%; colorless liquid; $^1$H NMR: $\delta$ = 1.20-1.95 (m, 12H), 3.81 (s, 3H), 5.72 (s, 2H); $^{13}$C NMR: $\delta$ = 24.86, 26.92, 31.68, 61.92, 103.92. Anal. calcd. for $C_9H_{17}NO_3$ (187.2): C, 57.74; H, 9.15. found: C, 58.12; H, 8.97.

**Reduction of 8d** with TPP gave **12d** as the sole product [$\delta$ 3.83 (s), 7.39 (s), 10.01 (s)].

***N*-Methoxy-3,4-dihydro-1,3-epidioxy-1H-2-benzoazine (11a)**: Yeild, 65%; colorless liquid; $^1$H NMR: $\delta$ = 2.91 (d, $J$ = 17.10 Hz, 1H), 3.10 (d, $J$ = 17.10 Hz, 1H), 3.48 (s, 3H), 5.42 (s, 1H), 5.69 (s, 1H), 7.68 (m, 4H); $^{13}$C NMR: $\delta$ = 37.68, 61.07, 94.67, 94.87, 126.11, 126.52, 128.28, 129.71, 130.56, 133.92. Anal. calcd. for $C_{10}H_{11}NO_3$ (193.2): C, 62.17; H, 5.74. found: C, 62.07; H, 5.57.

**Reduction of 11a** with TPP gave a mixture of **13a** and **14a** [$\delta$ 3.80 (s), 3.84 (s), 7.43 (m), 9.23 (s), 9.74 (s)].

***N*-Methoxy-4,5-dihydro-1,3-epidioxy-1H,3H-2-benzoazepine (11b)**: Yield, 35%; colorless liquid; $^1$H NMR: $\delta$ = 1.57 (m, 1H), 2.19 (m, 1H), 2.62 (m, 1H), 3.51 (m, 1H), 3.68 (s, 3H), 5.57 (d, $J$ = 6.31 Hz and 1.24 Hz, 1H), 6.00 (s, 1H), 7.20 (m, 4H); $^{13}$C NMR: $\delta$ = 28.31, 31.25, 61.33, 98.35, 103.28, 126.52, 128.52, 129.28, 130.28, 133.82. Anal. calcd. for $C_{11}H_{13}NO_3$(207.2): C, 63.76; H, 6.32. found: C, 63.55; H, 6.67.

**Reduction of 11b** with TPP gave a mixture of **13b** and **14b** [$\delta$ 3.84 (s), 3.94 (s), 7.43 (m), 9.74 (s), 10.16 (s)].

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