Formation of Ketone Diperoxides from Ozonation of *O*-Methyloximes

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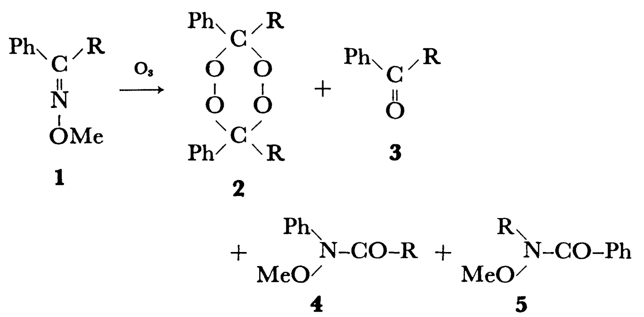
Synopsis. The ozonation of the *O*-methyloximes has been investigated. Besides the corresponding ketones, ketone diperoxides, and *N*-methoxyamides were produced. The stereochemistry of the ketone diperoxides was studied by the NMR technique.

In our previous paper,[1] it has been shown that the ozonation of valerophenone *O*-methyloxime (**1c**) in carbon tetrachloride at −20 °C gives as the major products valerophenone diperoxide (**2c**) and *N*-methoxyamides **4c** and **5c**, in addition to the corresponding ketone **3c**. Erickson *et al.*, however, reported[2] that the ozonation of acetophenone *O*-methyloxime (**1a**) in dichloromethane at −78 °C led to only the carbon–nitrogen double bond cleavage affording the corresponding ketone **3a**. This and our interest in a chemienergized process occurring from **2c**[3] led us to study the ozonation of *O*-methyloximes in more detail.



a: R=Me, **b**: R=Et, **c**: R=*n*-Bu, **d**: R=*t*-Bu

Scheme 1.

Table 1 shows the results of the ozonation of *O*-methyloximes **1a**—**d** in carbon tetrachloride or dichloromethane at low temperatures. In addition to the corresponding ketones **3a**—**d**, the ketone diperoxides **2a**—**c** and *N*-methoxyamides **4a**—**c** and **5a**—**d** were isolated, as we found previously.[1] In the case of **1d**, however, many by-products were also formed and only benzoic acid was characterizable.

The ketone diperoxides **2b** and **2c** were formed as a mixture of *cis* (**2b**-*c* and **2c**-*c*) and *trans* (**2b**-*t* and **2c**-*t*) isomers, while **2a** was obtained as a single isomer.[4] The yields of the *cis* and *trans* isomers were almost

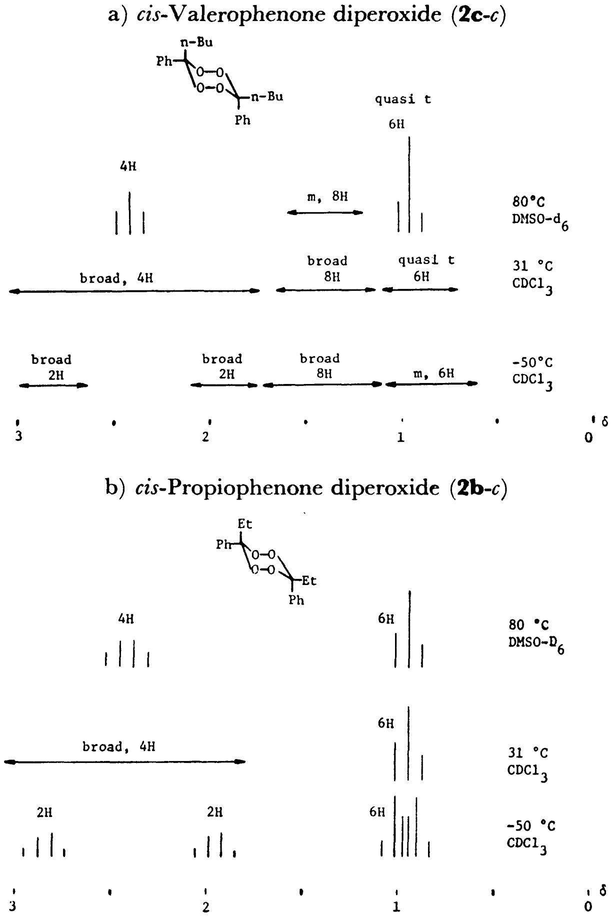


Fig. 1. NMR spectra (100 MHz) of *cis*-propiophenone diperoxide (**2b**-*c*) and *cis*-valerophenone diperoxide (**2c**-*c*) at different temperatures.

equal, *i.e.* **2b**-*t*/**2b**-*c*=1 and **2c**-*t*/**2c**-*c*=1.2. From their NMR spectra at a number of temperatures the higher melting isomers were assigned to be *trans* and the lower melting isomers to be *cis*. Similarly, the stereochemistry of acetophenone diperoxide (**2a**) was assigned to be *trans*.

The chair-to-chair conformational isomerism of acetone diperoxide was studied by Murray and coworkers by the NMR technique.[5] The NMR spectra

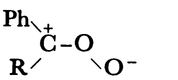
Table 1. The ozonation of *O*-methyl oximes **1** at low temperature

O-Methyloxime **1** (M×10²)	Solvent	O_3 passed (equiv)	Product (% yield)			
			2	**3**	**4**	**5**
1a (6.7)	CCl_4[a]	6.3	6	39	16	9
1a (8.0)	CH_2Cl_2[b]	57	10	43	11	8
1b (24.0)	CCl_4[a]	6.5	13[d]	51	11	10
1c (5.5)	CCl_4[a]	27	20[d]	34	13	16
1d (23.0)	CCl_4[c]	5.6	0	6	0	10[e]

a) At −20 °C. b) At −78 °C. c) At 0 °C. d) A combined yield of the *cis* and *trans* isomers. e) $PhCO_2H$ (15%) as a by-product.

of the *cis* isomers **2b**-*c* and **2c**-*c* (Fig. 1) indicated that they also underwent the conformational isomerization at room temperature and that the isomerization process was slowed down at low temperature (−50 °C) to the point where the chemical shifts of the axial and equatorial methylene groups can be discerned (Fig. 1. δ: **2b**-c_{eq} 2.85; **2b**-c_{ax} 1.96; **2c**-c_{eq} 2.78; **2c**-c_{ax} 1.92). According to Murray *et al.*,[5] the equatorial methylene group should be more deshielded (larger δ values). At 80 °C the peaks of the axial and equatorial methylene groups completely coalesced due to the rapid conformational isomerization (Fig. 1. δ: **2b**-*c* 2.42; **2c**-*c* 2.41). The *trans* isomers **2a**, **2b**-*t*, and **2c**-*t* showed essentially no dependency of their NMR spectra on temperatures between −50 °C and 140 °C, indicating that each of these *trans* isomers has a rigid conformation, as was found with other *trans* ketone diperoxides.[6] The alkyl substituents of the *trans* peroxides **2b**-*t* and **2c**-*t* can be regarded to be axial on the basis of the small δ values of the methylene groups adjacent to the tetroxane rings (δ: **2b**-*t* 1.62; **2c**-*t* 1.56).

The present reaction would be a convenient method for the preparation of ketone diperoxides which are not easily accessible. For example, we failed to prepare **2c** by the usual procedures for the synthesis of ketone diperoxides,[7] *i.e.*, from ozonolysis of 5,6-diphenyl-5-decene or from the reaction of valerophenone with hydrogen peroxide in the presence of sulfuric acid. As we have suggested previously,[1] a carbonyl oxide **6** seems to be a precursor of the ketone diperoxides **2**. In fact, when the ozonation of **1c** was carried out in the presence of excess acetaldehyde, the formation of **2c** was completely suppressed.[8] An oxaziridine **7** is the most probable intermediate of the *N*-methoxyamides **4** and **5**. Bailey *et al.* isolated the corresponding oxaziridine from the ozonation of *N*-benzylidene-*t*-butylamine in dichloromethane.[9]



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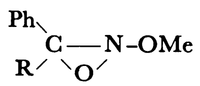

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Experimental

O-Methyloximes **1a**—**d** were prepared from the corresponding ketones and *O*-methylhydroxylamine hydrochloride according to the method of Karabatsos and Hsi.[10] Pivalophenone *O*-methyloxime (**1d**) was obtained as colorless crystals from ethanol, mp 64—66 °C. NMR ($CDCl_3$) δ 1.16 (9 H, s, *t*-Bu), 3.69 (3H, s, OCH_3), 6.8—7.6 (5H, m, ArH). IR (nujol) 1480, 1070, 880 cm^{-1}. MS *m/e* 191 (M^+, relative intensity 19), 175 (9), 160 (25), 104 (100), 77 (28), 57 (69), Found: C, 75.53; H, 9.13; N, 7.05%. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32%.

The ozonation and isolation procedures with **1c** were described previously.[1] Similar procedures were followed with **1a** (concentration 1.5 g/150 ml of CCl_4, ozonation time 2 h), **1b** (1.6 g/40 ml of CCl_4, 2 h), and **1d** (5.0 g/120 ml of CCl_4, 2 h). The physical and spectral properties of new substances are summarized below. The NMR and IR spectra of **2a**[11] and **5a**[12] were identical with those of the authentic sample.

4a. A colorless oil, bp 44.0—45.5 °C/0.1 mmHg. NMR ($CDCl_3$) δ 2.25 (3H, s, CH_3–CO), 3.66 (3H, s, CH_3O), 7.0—7.55 (5H, m, ArH). IR (neat) 1680 cm^{-1}. MS *m/e* 165 (M^+, 12), 122 (100), 77 (64), 43 (75). Found: C, 65.20; H, 6.70; N, 8.21%. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48%.

2b-*t*. Colorless crystals from acetone, mp 136.5—138 °C. NMR ($CDCl_3$ at 31 °C) δ 0.55 (6H, t, J=7 Hz, CH_3) 1.62 (4H, q, J=7 Hz, CH_2), 7.24—7.72 (10 H, m, ArH). The similar NMR spectra were obtained at −50 °C ($CDCl_3$), 80 °C (DMSO-d_6), and 140 °C (DMSO-d_6).

2b-*c*. A colorless viscous oil which resisted to crystallization. NMR ($CDCl_3$ at −50 °C) δ 0.91 (3H, t, J=7 Hz, CH_3), 1.01 (3H, t, J=7 Hz, CH_3), 1.96 (2H, q, J=7 Hz, CH_2), 2.85 (2H, q, J=7 Hz, CH_2), 7.02—7.90 (10H, m, ArH). ($CDCl_3$ at 31 °C) δ 0.94 (6H, t, J=7 Hz, CH_3), 1.8—3.1 (4H, broad, CH_2), 7.27 (10H, broad s, ArH). (DMSO-d_6 at 80 °C) δ 0.94 (6H, t, J=7.5 Hz, CH_3), 2.42 (4H, q, J=7.5 Hz, CH_2), 7.40 (10H, s, ArH).

4b. A colorless oil, bp 51—52 °C/0.1 mmHg. IR (neat) 1675 cm^{-1}. NMR ($CDCl_3$) δ 1.10 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 2.58 (2H, q, J=7 Hz, $CH_3C\underline{H}_2$), 3.70 (3H, s, CH_3O), 7.0—8.1 (5H, m, ArH). MS *m/e* 179 (M^+, 6), 57 (100). Found: C, 67.23; H, 7.52; N, 7.85%. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%.

5b. A colorless oil, bp 49—51 °C/0.1 mmHg. IR (neat) 1640 cm^{-1}. NMR ($CDCl_3$) δ 1.28 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 3.51 (3H, s, CH_3O), 3.72 (2H, q, J=7 Hz, $C\underline{H}_2$), 7.0—7.7 (5H, m, ArH). MS *m/e* 179 (M^+, 7), 105 (100), 77 (100). Found: C. 66.89; H, 7.52; N, 7.80%. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%.

5d. A colorless oil, bp 83—84 °C/0.1 mmHg. IR (neat) 1645 cm^{-1}. NMR ($CDCl_3$) δ 1.55 (9H, s, *t*-Bu), 3.35 (3H, s, CH_3O), 7.2—8.2 (5H, m, ArH). MS *m/e* 207 (M^+, 4), 105 (100), 77 (32), 57 (16). Found: C, 69.31; H, 8.29; N, 6.60%. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76%.

The physical and spectral properities of **2c**-*t*, **2c**-*c*, **4c**, and **5c** were reported Previously.[1] The temperature dependences of the NMR spectra of the *cis*-diperoxide **2c**—**c** and the *trans*-diperoxides **2c**-*t* and **2a** were analogous to those of **2b**-*c* and **2b**-*t*, respectively.

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