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Synthesis, structure and thermal decomposition of cycloalkanone enamine peroxides

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Reactions of cycloalkanone enamines with H_2O_2 gave bis(1-morpholinocyclopent-1-yl)- and bis(1-morpholinocyclohex-1-yl)-peroxides, which were studied by NMR spectroscopy and X-ray diffraction. Thermolysis of bis(1-morpholinocyclohex-1-yl)-peroxide in *n*-hexane resulted in two major products, *viz.*, cyclohexanone and morpholine.

The synthesis and chemical transformations of peroxides are of considerable interest. However, enamine peroxides were studied insufficiently. The synthesis of cycloalkanone enamine peroxides was reported in only one publication,[1] but the data provided in that publication seem unconvincing. The experimentally determined molecular masses differ by 25–30% from theoretical values. Almost no data are provided on the chemical transformations of these products.

In this work, we studied the reactions of cycloalkanone enamines with hydrogen peroxide in order to determine the structures of the resulting adducts and to explore the thermal decomposition of the latter.

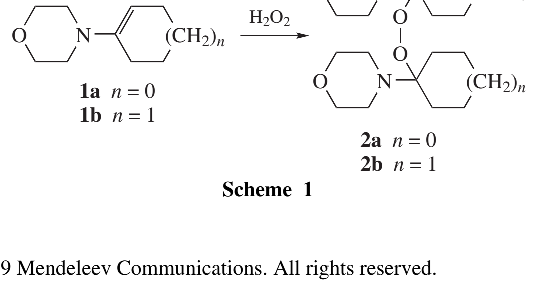
Reactions of appropriate amines and cycloalkanones in the presence of *p*-toluenesulfonic acid with azeotropic removal of water[2] resulted in the following enamines: 1-morpholinocyclopent-1-ene **1a**, 1-morpholinocyclohex-1-ene **1b**, 1-piperidinocyclopent-1-ene **1c**, 1-piperidinocyclohex-1-ene **1d** and 1-piperidinocyclohept-1-ene **1e**.[†]

Reactions of these enamines with aqueous and diethyl ether H_2O_2 solutions were studied. The use of aqueous H_2O_2 resulted in fast hydrolysis of the starting compounds, whereas the reaction with the diethyl ether solution allowed us to isolate individual bis(1-morpholinocyclopent-1-yl)peroxide **2a** and bis-(1-morpholinocyclohex-1-yl)peroxide **2b** (Scheme 1),[†] whose structures were determined by ^{1}H and ^{13}C NMR spectroscopy and X-ray diffraction analysis (XRD).

We obtained peroxides **2a** and **2b** as white crystalline compounds in 80–85% yields; the purity determined by ^{13}C NMR spectroscopy was 92–93%.

Enamines based on piperidine (**1c**–**e**) also react with diethyl ether H_2O_2 solutions to give peroxide products; however, we were unable to isolate them in a pure state as they were extremely unstable.

The structures of peroxides **2a** and **2b** were studied by XRD.[‡] The general view of the molecules of **2a** and **2b** along with selected geometrical parameters are presented in Figures 1 and 2.



Scheme 1

Note that, theoretically, peroxides **2** can have a wide variety of chemical structures. First, owing to the presence of cyclic fragments at carbon atoms located in the α-positions with respect to the peroxide group, the molecules of **2** are chiral and can

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[†] GLC analyses were carried out on an LKhM-80 chromatograph with a flame ionization detector using a 3 m×3 mm column with 6% SE-30 on Chromosorb W (60–80 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 instrument (200.13 MHz for ^{1}H and 50.32 MHz for ^{13}C). Melting points were determined in sealed capillaries.

The starting ketones and amines of 97–98% purity were purchased from Acros and Lancaster and used without further purification.

Enamines **1a**–**e** were obtained using a standard procedure[2] by boiling equimolar amounts of the reagents in benzene in the presence of *p*-toluenesulfonic acid with azeotropic removal of water.

Syntheses of peroxides. A starting enamine (0.03 mol) was placed in a stream of Ar into a flask equipped with a magnetic stirrer, and H_2O_2 (0.015 mol) was slowly added dropwise as a diethyl ether solution (17 ml); stirring was continued for another 45 min. The resulting peroxide was filtered off, washed with anhydrous diethyl ether and recrystallized from anhydrous diethyl ether at 10 °C.

1-Morpholinocyclopent-1-ene **1a**: bp 98 °C (8 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.75–1.95 (m, 2H, CH_2), 2.25–2.45 [m, 4H, $(CH_2)_2$], 2.80–2.95 [t, 4H, $(CH_2)_2N$], 3.60–3.75 [t, 4H, $(CH_2)_2O$], 4.35–4.45 (s, 1H, CH=C).

1-Morpholinocyclohex-1-ene **1b**: bp 108–109 °C (9 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.45–1.75 (br. m, 4H 2CH_2), 1.95–2.15 [m, 4H, $(CH_2)_2$], 2.65–2.80 [t, 4H, $(CH_2)_2N$], 3.65–3.75 [t, 4H, $(CH_2)_2O$], 4.60–4.70 (s, 1H, CH=C).

1-Piperidinocyclopent-1-ene **1c**: bp 109 °C (9 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.40–1.65 (br. m, 6H, 3CH_2), 1.75–2.0 (m, 2H, CH_2), 2.25–2.45 [m, 4H, $(CH_2)_2$], 2.75–2.95 [t, 4H, $(CH_2)_2N$], 4.75–4.85 (s, 1H, CH=C).

1-Piperidinocyclohex-1-ene **1d**: bp 120 °C (9 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.40–1.75 (br. m, 10H, 5CH_2), 1.80–2.00 [m, 4H, $(CH_2)_2$], 2.15–2.85 [t, 4H, $(CH_2)_2N$], 4.75–4.86 (s, 1H, CH=C).

1-Piperidinocyclohept-1-ene **1e**: bp 124 °C (8 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.35–1.72 (br. m, 12H, 6CH_2), 2.2–2.35 (m, 4H, 2CH_2), 2.55–2.60 [t, 4H, $(CH_2)_2N$], 4.72–4.80 (s, 1H, CH=C).

Bis(1-morpholinocyclopent-1-yl)peroxide **2a**: bp 84–86 °C. ^{1}H NMR ($CDCl_3$) δ: 2.65–3.00 [br. m, 4H, $(CH_2)_2N$], 3.55–3.90 [m, 4H, $(CH_2)_2O$]. ^{13}C NMR ($CDCl_3$) δ: 23.52 (s, CH_2CH_2), 34.62 (s, CH_2–C–CH_2), 48.75 (s, CH_2N), 67.57 (s, CH_2O), 106.25 (s, CON). The product purity is 93%, according to ^{13}C NMR data.

Bis(1-morpholinocyclohex-1-yl)peroxide **2b**: bp 98–99 °C. ^{1}H NMR ($CDCl_3$) δ: 1.4–2.0 (br. m, 10H, 5CH_2), 2.70–2.90 [m, 4H, $(CH_2)_2N$], 3.60–3.80 [br. m, 4H, $(CH_2)_2O$]. ^{13}C NMR ($CDCl_3$) δ: 22.18 (CH_2), 25.63 (CH_2), 29.46 (CH_2), 46.01 (CH_2N), 67.75 (CH_2O), 95.65 (CON). The product purity is 94%, according to ^{13}C NMR data.

exist as six different isomers (the conformations of substituents at carbon atoms located in the α-positions with respect to the peroxide group are shown):

Two *meso*-forms: $t_N/g_C^{(+)}\text{-}g_C^{(-)} - t_N/g_C^{(-)}\text{-}g_C^{(+)}$
$g_N^{(+)}/t_C\text{-}g_C^{(-)} - g_N^{(-)}/t_C\text{-}g_C^{(+)}$

Four *d*,*l*-forms: $t_N/g_C^{(+)}\text{-}g_C^{(-)} - g_N^{(+)}/t_C\text{-}g_C^{(-)}$
$t_N/g_C^{(+)}\text{-}g_C^{(-)} - g_N^{(-)}/t_C\text{-}g_C^{(+)}$
$g_N^{(+)}/t_C\text{-}g_C^{(-)} - g_N^{(+)}/t_C\text{-}g_C^{(-)}$
$g_N^{(-)}/t_C\text{-}g_C^{(+)} - g_N^{(-)}/t_C\text{-}g_C^{(+)}$

However, the g_C-g_C conformation of saturated carbon cycles with respect to the peroxide group is sterically unfavourable; hence, an experiment is most likely to show the formation of only three of the isomers specified above, namely, one *meso*-form ($g_N^{(+)}/t_C\text{-}g_C^{(-)} - g_N^{(-)}/t_C\text{-}g_C^{(+)}$) and two *d*,*l*- forms ($g_N^{(+)}/t_C\text{-}g_C^{(-)} - g_N^{(+)}/t_C\text{-}g_C^{(-)}$ and $g_N^{(-)}/t_C\text{-}g_C^{(+)} - g_N^{(-)}/t_C\text{-}g_C^{(+)}$). In fact, all the three isomers are actually formed in compounds **2a** (both *d*,*l*-forms) and **2b** (*meso*-form). While compound **2a** is crystallized as a racemate of enantiomers of both isomers (space group *C*2/*c*), compound **2b** either forms only the *meso*-form, or its isomers are spontaneously separated from each other upon crystallization (space group $P2_1$). The assumption that compound **2b** can exist only as a *meso*-form follows from the fact that, apparently, due to steric factors, an increase in the size of cycloalkane substituents at the carbon atoms in α-positions with respect to the peroxide group should favour the formation of the *meso*-form.

Second, isomers of peroxides **2** can also form various conformers. Note that the experimentally observed isomers of peroxide **2a** are different conformers with respect to the orientation of five-membered rings, which have an envelope conformation typical of such fragments. In fact, in one of the isomers, it is the C(4) atom in the β-position to the C(1) nodal carbon atom which deviates from the plane formed by the other four atoms in both five-membered rings, whereas in the other isomer, it is the C(10) nodal atom (Figure 1). In the latter case, the morpholine substituents occupy the equatorial positions, whereas the peroxide group is axial. Furthermore, the *meso*-form of compound **2b** observed in a crystal also has an unusual conformation with respect to the mutual orientation of the cyclohexane fragments. While one of the cyclohexane fragments contains a peroxide group in an equatorial position and a morpholine substituent in an axial position, the other fragment, conversely, contains a morpholine substituent in an equatorial position and a peroxide group in an axial position (Figure 2). Apparently, a superposition of the two geometrical factors described above gives a single enantiomer of compound **2b**; as a result, crystallization of this compound occurs in chiral space group $P2_1$. It should be noted that both factors can act independently of each other and can depend on the kinetic conditions of the reaction.

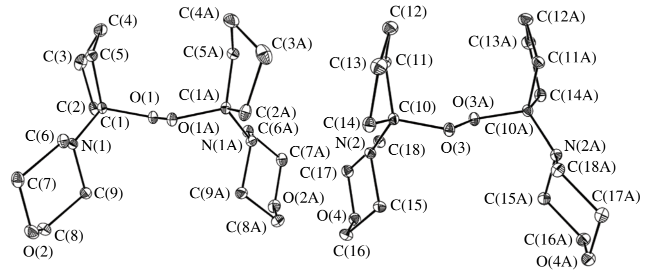

Figure 1 Molecular structure of **2a**; hydrogen atoms are omitted for clarity; two independent molecules representing the different conformers are shown. Labels A denote symmetrically equivalent atoms relative to the 2-fold axis. Selected bond lengths (Å) and angles (°): O(1)–O(1A) 1.482(3), O(3)–O(3A) 1.486(3), O(1)–C(1) 1.459(2), O(3)–C(10) 1.457(2), N(1)–C(1) 1.442(3), N(1)–C(6) 1.469(2), N(1)–C(9) 1.465(3), N(2)–C(10) 1.443(3), N(2)–C(15) 1.461(3), N(2)–C(18) 1.467(3); O(1A)–O(1)–C(1) 108.1(2), O(3A)–O(3)–C(10) 108.0(2), N(1)–C(1)–O(1) 114.2(2), N(2)–C(10)–O(3) 114.4(2), O(1)–C(1)–C2 100.6(2), O(1)–C(1)–C(5) 110.3(2), O(3)–C(10)–C(11) 110.8(2), O(3)–C(10)–C(14) 100.7(2), C(1)–N(1)–C(6) 118.2(2), C(1)–N(1)–C(9) 114.0(2), C(6)–N(1)–C(9) 109.1(2), C(10)–N(2)–C(15) 114.5(2), C(10)–N(2)–C(18) 117.0(2), C(15)–N(2)–C(18) 109.1(2), C(1)–O(1)–O(1A)–C(1A) –156.4(2), C(10)–O(3)–O(3A)–C(10A) 158.9(2), O(1A)–O(1)–C(1)–N(1) –59.1(2), O(3A)–O(3)–C(10)–N(2) –66.6(2), O(1A)–O(1)–C(1)–C(2) –179.1(1), O(1A)–O(1)–C(1)–C(5) 69.9(2), O(3A)–O(3)–C(10)–C(11) –63.0(2), O(3A)–O(3)–C(10)–C(14) –172.4(1).

It is interesting that, despite the different structures of compounds **2a** and **2b**, the geometric characteristics of their main peroxide C–O–O–C fragment are rather similar. This fragment deviates slightly from an ideal planar structure [the torsion angles are –156.4(2) and 158.9(2)° for **2a** and –170.6(3)° for **2b**]; this deviation is more significant for compound **2a**, as

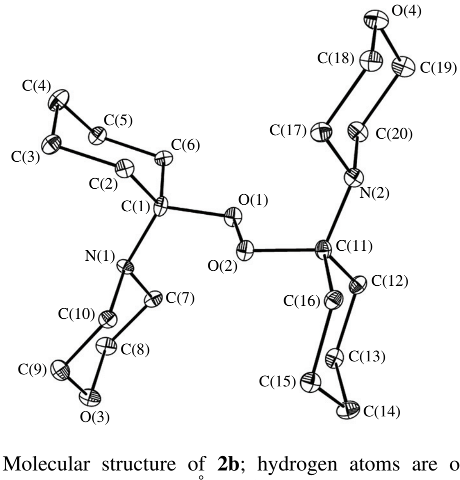

Figure 2 Molecular structure of **2b**; hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): O(1)–O(2) 1.497(3), O(1)–C(1) 1.455(4), O(2)–C(11) 1.458(4), N(1)–C(1) 1.454(4), N(1)–C(7) 1.461(4), N(1)–C(10) 1.473(4), N(2)–C(11) 1.451(4), N(2)–C(17) 1.467(4), N(2)–C(20) 1.481(5); O(1)–O(2)–C(11) 106.4(2), O(2)–O(1)–C(1) 108.7(2), N(1)–C(1)–O(1) 113.7(3), N(2)–C(11)–O(2) 114.0(3), O(1)–C(1)–C(2) 111.1(3), O(1)–C(1)–C(6) 101.1(3), O(2)–C(11)–C(12) 111.0(3), O(2)–C(11)–C(16) 100.6(3), C(1)–N(1)–C(7) 115.6(3), C(1)–N(1)–C(10) 117.2(3), C(7)–N(1)–C(10) 108.7(3), C(11)–N(2)–C(17) 115.7(3), C(11)–N(2)–C(20) 118.0(3), C(17)–N(2)–C(20) 107.4(3), C(1)–O(1)–O(2)–C(11) –170.6(3), O(1)–O(2)–C(11)–N(2) 71.2(3), O(2)–O(1)–C(1)–N(1) –77.6(3), O(1)–O(2)–C(11)–C(12) –56.0(3), O(1)–O(2)–C(11)–C(16) –171.8(2), O(2)–O(1)–C(1)–C(2) 49.4(3), O(2)–O(1)–C(1)–C(6) 163.6(2).

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‡ *Crystal data for* **2a**: $C_{18}H_{32}N_2O_4$, $M = 340.46$, monoclinic, space group *C*2/*c*, at 120 K: $a = 22.346(3)$, $b = 14.313(2)$ and $c = 15.556(2)$ Å, $\beta = 134.008(2)°$, $V = 3578.5(8)$ Å^3, $Z = 8$, $d_{calc} = 1.264$ g cm^{-3}, $F(000) = 1488$, $\mu = 0.089$ mm^{-1}, $R_1 = 0.059$ for 3003 independent reflections with $I > 2\sigma(I)$, $wR_2 = 0.177$ for all data, GOF = 1.028. 15854 reflections (3771 unique, $R_{int} = 0.037$) were measured on a Bruker SMART 1K CCD diffractometer (MoKα-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max} = 54°$).

Crystal data for **2b**: $C_{20}H_{36}N_2O_4$, $M = 368.51$, monoclinic, space group $P2_1$, at 100 K: $a = 10.7044(14)$, $b = 6.2298(8)$ and $c = 14.517(2)$ Å, $\beta = 91.407(3)°$, $V = 967.8(2)$ Å^3, $Z = 2$, $d_{calc} = 1.265$ g cm^{-3}, $F(000) = 404$, $\mu = 0.087$ mm^{-1}, $R_1 = 0.050$ for 1469 independent reflections with $I > 2\sigma(I)$, $wR_2 = 0.106$ for all data, GOF = 1.005. 9706 reflections (2180 unique, $R_{int} = 0.062$) were measured on a Bruker SMART 1K CCD diffractometer (MoKα-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max} = 53°$).

The structures were determined by direct methods and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined in the riding model with fixed isotropic displacement parameters. All calculations were carried out using the SHELXTL program.[3]

CCDC 745598 and 745599 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

one could have expected for *d*,*l*-isomers. The O–O bond length and the O–O–C bond angles have values typical of peroxide molecules with similar structures.[4]

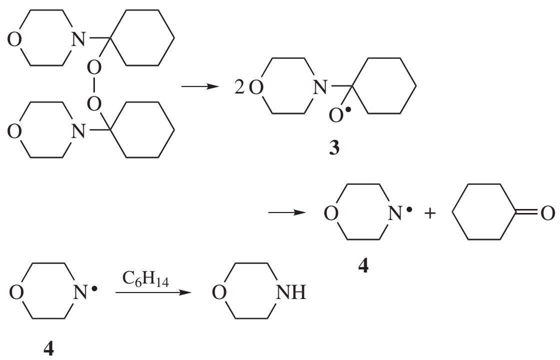
Note a structural feature of the compounds studied, namely, the *trans*-effect well known for peroxides, which involves distortion of the tetrahedral coordination of quaternary carbon atoms bound to oxygen atoms.[5] In molecules of **2a** and **2b**, the O–C–C bond angles in the *trans*-position to the O–O peroxide group decrease in comparison with an ideal tetrahedral angle of 109.5° down to 100.6(2), 100.7(2) and 101.1(3), 100.6(3)°, respectively. The six-membered morpholine and cyclohexane fragments have an almost ideal chair conformation.

In addition to the structures of peroxides **2a** and **2b**, we also studied the thermal decomposition of bis(1-morpholinocyclohexyl)peroxide **2b**. Thermolysis of a 6% solution of peroxide **2b** in *n*-hexane was carried out at 60 °C in a sealed glass tube for 6 h until the peroxide decomposed completely.

It was found that cyclohexanone and morpholine were the main thermolysis products of compound **2b**; these products were formed in 40 and 30% yields, respectively (on a starting peroxide basis) as determined by GLC with the use of internal standards.

Based on these data, it can be assumed that the reaction mechanism involves homolysis of the O–O bond accompanied by generation of alkoxy radicals **3**, which subsequently undergo a β-decomposition to give cyclohexanone and morpholyl N-radicals **4**. The latter abstract a hydrogen atom from the solvent to give morpholine (Scheme 2).

This homolytic decomposition mechanism of bis(1-morpholinocyclohexyl)peroxide appears most probable; however, it does not rule out alternative pathways.



Scheme 2

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