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Spontaneous formation and stabilization of radicals during the cocrystallization of alicyclic and peroxyalicyclic dicarboxylic acids

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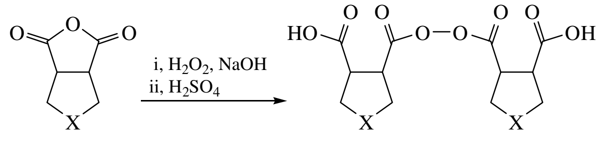
The cocrystallization of di(*cis*-2-carboxycyclohexylcarbonyl) peroxide and cyclohexane-1,2-dicarboxylic acid from aqueous solution affords stable 1-carboxycyclohexyl radicals, which were identified by EPR spectroscopy.

Radicals are generally generated by physical (thermolysis, photolysis, radiolysis or electric discharge) or chemical (RedOx systems) action.[1]

In the 1980s, we discovered the formation and stabilization of carbon-centered radicals during the cocrystallization of aliphatic peroxydicarboxylic (peroxysuccinic and peroxyglutaric) acids with dicarboxylic (succinic, glutaric and fumaric) acids without any additional action on the resulting crystalline system. The radicals thus generated occur in a solid matrix, which hinders diffusion. In such matrices, these radicals remain intact at room temperature for several months.[2–4]

These radicals are of scientific and practical interest because they are initiators for low-temperature polymerization, telomerization and vulcanization. We believe that this phenomenon is of a general character and can be extended to other organic peroxides. To confirm this expectation, we performed the reactions of anhydrides **1a**,**b** with hydrogen peroxide in an alkaline medium to prepare di(*cis*-2-carboxycyclohexylcarbonyl) peroxide **2a** and di(*cis*-2-carboxycyclohexenylcarbonyl) peroxide **2b** (Scheme 1), respectively, and then carried out the cocrystallization of these products with *cis*-cyclohexane-1,2-dicarboxylic **3a**[5] and *cis*-cyclohex-4-ene-1,2-dicarboxylic **3b**[6] acids, respectively.[†]

Peroxides **2a** and **2b** were characterised by IR, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis; acids **3a** and **3b**, by NMR spectroscopy.[‡]



1a,**b** **2a**,**b**

a X = $CH_2–CH_2$
b X = CH=CH

Scheme 1

The IR spectra show absorption bands at 1080 and 1060 cm^{-1} assigned to vibrations of the peroxide (O–O) group.[7]

The ^{13}C NMR spectrum of peroxide **2a** shows two signals of the carboxy [δ 174.2 (s, COOH)] and peroxide [δ 174 (s, COOO)] groups. The ^{13}C NMR spectrum of peroxide **2b** also has two signals at δ 174.2 (s, COOH) and 169.7 (s, COOO). Note that the ^{13}C NMR spectrum of peroxide **2b** exhibits two signals of the C=C group at δ 125 and 126, whereas the spectrum of dicarboxylic acid **3b** shows one singlet of the C=C bond at δ 126. The observed nonequivalence is, apparently, associated with the influence of the peroxide bond of **2b**, resulting in a lowering of the molecular symmetry.

Earlier, X-ray diffraction studies showed that the structural similarity of the starting compounds is one of the main prerequisites for the formation of stabilised radicals during the cocrystallization of peroxysuccinic and succinic acids or peroxyglutaric and glutaric acids.[8,9] The peroxide molecule, which is bulkier than the corresponding two dicarboxylic acid molecules, is inserted into the crystalline lattice of the dicarboxylic acid matrix, and the O–O bond cleavage in peroxide occurs as a result of deformation strain in the crystalline lattice.[4]

The EPR study showed that the cocrystallization of peroxide **2a** with dicarboxylic acid **3a**[§] affords radical species. The primary EPR spectrum of the cocrystallization product is a superposition of an unresolved singlet with $g_{\mathrm{i}} = 2.0053$ and a

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[†] The starting *cis*-cyclohexane-1,2-dicarboxylic anhydride **1a** and *cis*-cyclohex-4-ene-1,2-dicarboxylic anhydride **1b** (Aldrich) were used without additional purification. A finely ground powder of the anhydride (0.01 mol) was added with vigorous stirring to 3% H_2O_2 (30 ml) and 10% NaOH (15 ml) at –3–4 °C in such a way that the temperature was no higher than 2 °C. The reaction mixture was filtered, and the solution was acidified with 10% H_2SO_4 to pH ~ 2. The peroxide was separated by filtration, washed with cold distilled water and dried in a vacuum desiccator. The yields of **2a** and **2b** were 15 and 10%, respectively. Both peroxides are readily soluble in water, methanol and acetone and are poorly soluble in benzene. Acids **3a** and **3b** were synthesised by the reactions of anhydrides **1a** and **1b**, respectively, with a 20% NaOH solution at 5 °C followed by acidification with 10% H_2SO_4 to pH ~ 2. The resulting acids were filtered off, washed with cold distilled water and dried.

[‡] The NMR spectra were recorded on a Bruker AC-200 spectrometer (200.13 MHz for ^{1}H and 50.32 MHz for ^{13}C). The IR spectra were measured on a Specord M-82 instrument.

2a: mp 94–95 °C. ^{1}H NMR [$(CD_3)_2CO$] δ: 1.5 (m, 4H, CH_2CH_2), 1.85 (m, 4H, C*H*$_2$CHCOOH, C*H*$_2$CHCOO), 2.9 (m, 1H, C*H*COOH), 3.1 (m, 1H, CHCOO). ^{13}C NMR {H} [$(CD_3)_2CO$] δ: 174.2 (s, COOH), 174.0 (s, COOO), 42.4 (s, *C*HCOOH), 40.6 (s, *C*HCOO), 26.4 (s, *C*H$_2$CHCOOH), 24.0 (s, *C*H$_2$CHCOOO), 23.95 (s, CH_2CH_2). IR (vaseline oil, ν/cm^{-1}): 1804, 1776, 1696, 1080, 1060. Found (%): C, 56.18; H, 6.40. Calc. for $C_{16}O_8H_{22}$ (%): C, 56.14; H, 6.43.

2b: mp 89–90 °C. ^{1}H NMR [$(CD_3)_2CO$] δ: 2.2–2.7 (br. m, 4H, C*H*$_2$CHCOOH, C*H*$_2$CHCOO), 3.08 (m, 1H, CHCOO), 3.23 (m, 1H, CHCOO), 5.67 (m, 2H, CH=CH). ^{13}C NMR {H} [$(CD_3)_2CO$] δ: 174.19 (s, COOH), 169.7 (s, COOO), 126.16 and 124.88 (2s, CH=CH), 39.76 (s, *C*HCOOH), 37.06 (s, *C*HCOO), 26.39 and 26.19 (2s, 2CH$_2$). IR (vaseline oil, ν/cm^{-1}): 1804, 1776, 1760, 1660, 1080, 1060. Found (%): C, 56.69; H, 5.58. Calc. for $C_{16}O_8H_{18}$ (%): C, 56.69; H, 5.46.

3a: ^{1}H NMR [$(CD_3)_2CO$] δ: 1.5 (m, 2H, CH$_2$), 2.1–1.8 (m, 2H, C*H*$_2$CHCOOH), 2.85 (m, 1H C*H*COOH). ^{13}C NMR {H} [$(CD_3)_2CO$] δ: 174.95 (s, COOH), 42.47 (s, *C*HCOOH), 26.7 (s, *C*H$_2$CHCOOH), 26.19 (s, CH$_2$).

3b: ^{1}H NMR [$(CD_3)_2CO$] δ: 2.3–2.6 (m, 2H, CH$_2$), 3.02 (m, 1H, C*H*COOH), 5.64 (m, 2H, CH=CH). ^{13}C NMR {H} [$(CD_3)_2CO$] δ: 175.08 (s, COOH), 126.00 (s, CH=CH), 26.60 (s, CH$_2$).

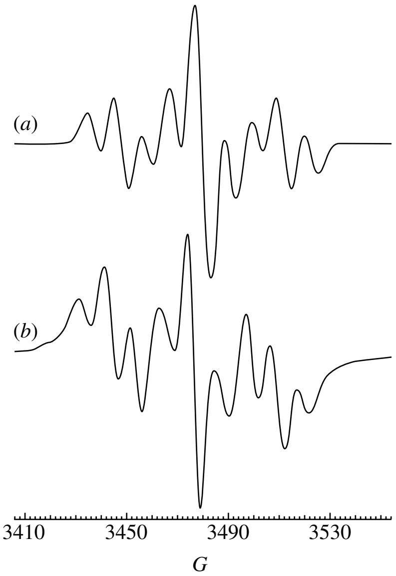
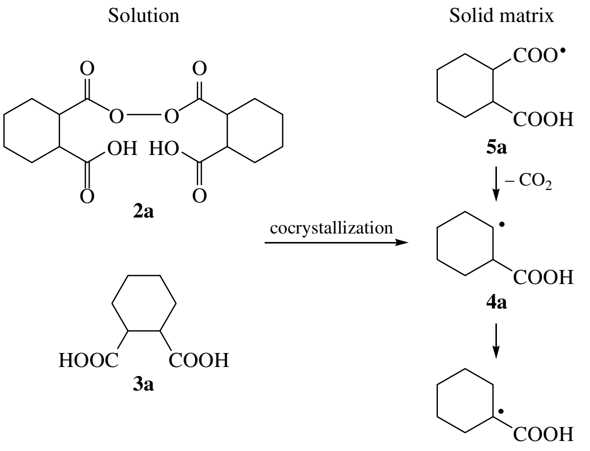


Figure 1 (*a*) Simulated spectrum for **5a** and **6a** radicals (line width = 7, *L*/*G* = 1) and (*b*) experimental EPR spectrum.

triplet of triplets with the parameters $g_\mathrm{i} = 2.0029$, $A_\mathrm{i}(^1\mathrm{H}) = 32$ G, $A_\mathrm{i}(^1\mathrm{H}) = 10$ G and the linewidth of about 7 G, which is apparently attributed to interactions with the matrix substance. The central singlet disappears in a few hours, and the triplet of triplets becomes more pronounced, the parameters remain unchanged (Figure 1).

Most likely, the singlet, whose intensity decreases much more rapidly than that of the triplet of triplets, belongs to acyloxy radical **5a**, which is additionally confirmed by the value of g_i. According to PBE calculations[10] with the TZ2P basis set[11] using the PRIRODA program,[12] radical **5a** has small splitting constants ($\leq$ 1.5 G), which do not allow us to observe the resolved signal. The second spectrum, the triplet of triplets, is assigned to 1-carboxycyclohexyl radical **6a**. In the crystalline lattice, these radicals are packed so that there are two pairs of nonequivalent (axial and equatorial) β-protons with the hyperfine coupling constants $A_\mathrm{i}(^1\mathrm{H}) = 32$ G and $A_\mathrm{i}(^1\mathrm{H}) = 10$ G. This is also confirmed by quantum chemical calculations, as well as small ($\leq$1.7 G) splitting constants for all other protons. All other possible radicals definitely have completely different calculated splitting constants.



Scheme 2

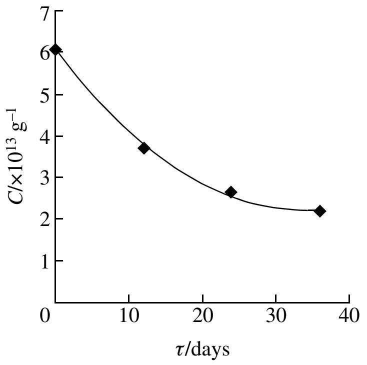
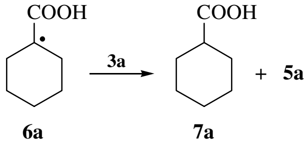


Figure 2 Plot of the concentration of the radicals *vs.* time.

Therefore, the mechanism of formation of radical **6a** by the cocrystallization of peroxide **2a** with dicarboxylic acid **3a** can be represented by Scheme 2.

Radicals **4a** that are initially generated from peroxide **2a** are rearranged into more stable EPR-detectable radicals **6a** *via* the 1,2-migration of the hydrogen atom.

Radicals **6a** abstract hydrogen from the matrix substance, dicarboxylic acid **3a**, thus being transformed into cyclohexanecarboxylic acid **7a** (Scheme 3). The latter was extracted from the reaction mixture with hexane and then methylated with diazomethane. The methyl ester was identified by chromatography–mass spectrometry.



Scheme 3

To study the cocrystallization products of dicarboxylic acid **3a** with peroxydicarboxylic acid **2a** by EPR, six samples with different ratios between the starting compounds (4–90%) were prepared. For these samples, the disappearance rate of radicals was followed for 1.5 months. The molar concentration of the peroxide optimal for stabilization of the radicals in the solid matrix was found to be 40% with respect to dicarboxylic acid. The measured initial concentration of the radical species in this sample was about 10^{14} g^{-1}. Figure 2 presents the concentration *vs.* time for a sample stored at room temperature.

The cocrystallization products of peroxide **2b** and peroxydicarboxylic acid **3b** (4–90% **3b**) were also studied by EPR spectroscopy. In this case, the spectrum range corresponds to that of radical **5a**. However, a pronounced multiplet pattern was not observed.

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[§] *Cocrystallization.* Peroxydicarboxylic acid **2a** (**2b**) and dicarboxylic acid **3a** (**3b**) were completely dissolved in a required amount of distilled water, the solvent was distilled off and the solid residue was dried in a vacuum desiccator. The peroxide content was determined by iodometric titration.

The EPR spectra were recorded on a Bruker EMX 6/1 spectrometer equipped with an ER-4102ST resonator (9.8 GHz) and an ER 4111 VT temperature controlling unit; dpph was used as a standard for the determination of the *g* factors.

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