

Hydrogen Atom Transfer in Photolyzed (*S,S*)-Bis(13-bromo-2-deuteriotridecanoyl) Peroxide: Control of Regiospecificity by Crystal Chirality

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As part of a broader study of radical reactions in single crystals, which is aimed at exploring factors that influence reactions in structured environments,¹ we have investigated a series of exquisitely specific hydrogen atom transfers in solid bis(11-bromoundecanoyl) peroxide (BrUP). These reactions were ob-

$\text{Br}(\text{CH}_2)_n\text{CO}_2\text{O}_2\text{C}(\text{CH}_2)_n\text{Br}$

BrUP, $n = 10$; BrTP, $n = 12$

served by EPR spectroscopy after warming of a BrUP crystal in which an initial pair of primary 10-bromodecyl radicals had been generated in low concentration by photochemical double decarboxylation below 80 K.^{1b,2} This communication reports two of the hydrogen transfers and describes how crystal chirality was used to help study them.

At 100 K the first hydrogen transfer gives a radical pair, pair- α , with a spectrum (Figure 1a) that we attribute to splitting by seven protons, 21 G (2 H), 24 G (3 H), 25 G (1 H), 39 G (1 H), in addition to an electron-electron zero-field splitting (zfs) of 47 G.³ The high symmetry of crystalline BrUP requires eight identical, but differently oriented, versions of pair- α .⁴ Without deuteration the overlapped spectra are impossible to unscramble, except when the magnetic field is along the tetrad axis so that all eight spectra are identical, as in Figure 1a.

To identify the radicals in pair- α and to infer their arrangement from zfs anisotropy, we studied variously deuterated crystals of BrUP and, for synthetic convenience, of bis(13-bromotridecanoyl) peroxide (BrTP), which has an analogous crystal structure and gives the same series of reactions.⁵ Dideuteration of the β -methylene groups in both chains of BrTP removed four splittings from the spectrum (39 G, 25 G, and two of 24 G; Figure 1b). The simplification allowed estimation of electron-electron splittings in poorly resolved spectra for 31 different crystal orientations to yield an approximate zfs tensor. Zfs indicated an 8.5 (5) Å spin-spin vector approximately bisecting the angle between the a and b axes of the unit cell. Together with the hyperfine splitting, this suggested strongly that one of the primary radicals in the initial pair abstracts hydrogen from a particular α -carbon of a neighboring intact peroxide molecule (Figure 2a).⁶ Pair- α thus consists of a primary radical and a secondary α radical.

A sample with α -deuteration should confirm this assignment. However, crystals of BrUP with complete α -deuteration, or α - and β -deuteration, did not yield pair- α . Instead the pair of primary radicals survived to 140 K, whereupon the two samples gave identical spectra with splitting by 10 protons⁷ in addition to a 77-G zfs (Figure 1d). In a crystal of BrTP completely deuterated in the α - and γ -positions, four of the proton splittings disappeared (Figure 1e). This simplification and the electron-electron zfs⁸

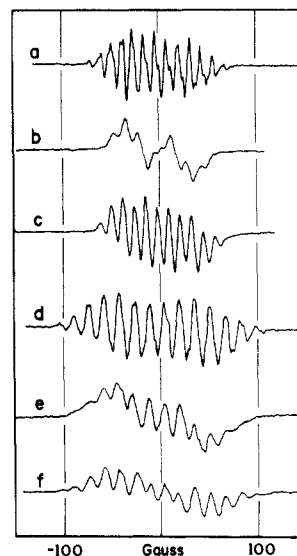


Figure 1. EPR spectra measured with magnetic field along (001): (a) pair- α , $\text{Br}(\text{CH}_2)_8\text{CH}_2\text{C}^*\text{H}_2/\text{XC}^*\text{HCH}_2(\text{CH}_2)_8\text{Br}$; (b) pair- α , $\text{Br}(\text{CH}_2)_{10}\text{CD}_2\text{C}^*\text{H}_2/\text{XC}^*\text{HCD}_2(\text{CH}_2)_{10}\text{Br}$; (c) pair- α , $\text{Br}(\text{CH}_2)_{10}\text{CH}_2\text{C}^*\text{HD}/\text{XC}^*\text{DCH}_2(\text{CH}_2)_{10}\text{Br}$; (d) pair- δ , $\{\text{Br}(\text{CH}_2)_5\text{CH}_2\text{C}^*\text{HCH}_2\text{CH}_2\text{CD}_2\text{X}\}_2$; (e) pair- δ , $\{\text{Br}(\text{CH}_2)_7\text{CH}_2\text{C}^*\text{HCH}_2\text{CH}_2\text{CHDX}\}_2$; (f) pair- δ , $\{\text{Br}(\text{CH}_2)_7\text{CH}_2\text{C}^*\text{HCH}_2\text{CH}_2\text{CHDX}\}_2$; where $\text{X} = \text{CO}_2\text{O}_2\text{CR}$.

indicate that both primary radicals specifically abstract corresponding δ -hydrogens from adjacent molecules to give pair- δ , a pair of secondary radicals (Figure 2d).⁹

The primary radicals avoid α -deuterium, preferring to abstract unactivated δ -protium, at a temperature 40 K above that at which α -protium is abstracted with a comparable rate.

The kinetic isotope effect prevented preparing α -deuterated pair- α from peroxide with α,α -dideuterated chains, but it could be avoided with specifically monodeuterated chains containing protium in position to be transferred. Although in solution the geminal α -hydrogens are only enantiotopic, in the crystal the frozen molecular conformation and fixed environment make them diastereotopic. Since $P4_1(3)2_12$ lacks improper symmetry elements, all sites in a single BrUP crystal have the same handedness. If the proposed mechanism is correct, primary radical pairs in a $P4_22_1$ crystal of bis-monodeuterated BrUP (or BrTP) with the S,S configuration should undergo transfer of "equatorial" α -hydrogen to give pair- α (Figure 2a).¹⁰ In the enantiomorphic space group the same substance will have equatorial deuterium, and isotopic retardation should result in formation of pair- δ (Figure 2d).

From 100 mg of (*S,S*)-bis(13-bromo-2-deuteriotridecanoyl) peroxide in methylene chloride/ethyl acetate/hexanes, 11 single crystals were grown in one batch.¹¹ Anomalous X-ray scattering from five of these crystals was analyzed to show that each one had space group $P4_22_1$.¹² After photolysis at 77 K and annealing to 120 K, each of the 11 crystals gave the desired EPR spectrum of pair- α , simplified by removal of one 24-G and one 21-G splitting and broadened by unresolved deuterium coupling (Figure 1c).

These observations confirm the structure of pair- α and the mechanism of its formation.

Analogous crystallization in the enantiomorphic space group was achieved by seeding¹³ and confirmed by X-ray diffraction.

(8) Positions of the δ -carbons in the starting material predict a splitting of 75.3 G for this crystal orientation.

(9) The initial H-C-C* distance for δ transfer is 3.33 Å; the C₂-H-C* angle, 123°. For the moved radical (Figure 2) the values are 3.04 Å, 150°.

(10) We use "axial" to denote CH bonds parallel to the molecular dyad (the line of sight in Figure 2). The equatorial H-C-C* distance is 3.10 Å; the C₂-H-C* angle, 151° (3.03 Å, 159° for moved radical). The axial values are 4.24 Å and 78°.

(11) Synthesis of this compound, which involved Sharpless epoxidation of 2,12-tridecadien-1-ol and LiAlD₄ displacement of a protected tosylate, is described in the following: Feng, X. W. Ph.D. Thesis, Yale University, 1989.

(12) We thank Dr. S. B. Bertman for making these measurements using the methods of ref 4.

(1) (a) McBride, J. M. *Acc. Chem. Res.* 1983, 16, 304. (b) McBride, J. M.; Segmuller, B. E.; Hollingsworth, M. D.; Mills, D. E.; Weber, B. A. *Science* 1986, 234, 830. (c) Hollingsworth, M. D.; McBride, J. M. *Adv. Photochem.* 1990, 15, 279.

(2) Mills, D. E. Ph.D. Thesis, Yale University, 1986.

(3) The observed hyperfine separations are half of these values because of strong spin exchange in the radical pair. Radical-pair EPR is discussed in the following: McBride, J. M.; Vary, M. W.; Whitsel, B. L. *Organic Free Radicals*; ACS Symposium Series 69; American Chemical Society: Washington, DC, 1978; p 208.

(4) Space group $P4_1(3)2_12$. McBride, J. M.; Bertman, S. B.; Cioffi, D. Z.; Segmuller, B. E.; Weber, B. A. *Mol. Cryst. Liq. Cryst.* 1988, 161, 1.

(5) This compound was first described by Mills.² Its crystal structure was determined by S. B. Bertman (unpublished).

(6) In the starting crystal the carbons which become the radical centers of pair- α are related by unit translation along a and b , a distance of 7.7 Å.

(7) Simulated by two protons each with hfs of 27, 28, 31, 33, and 39 G.

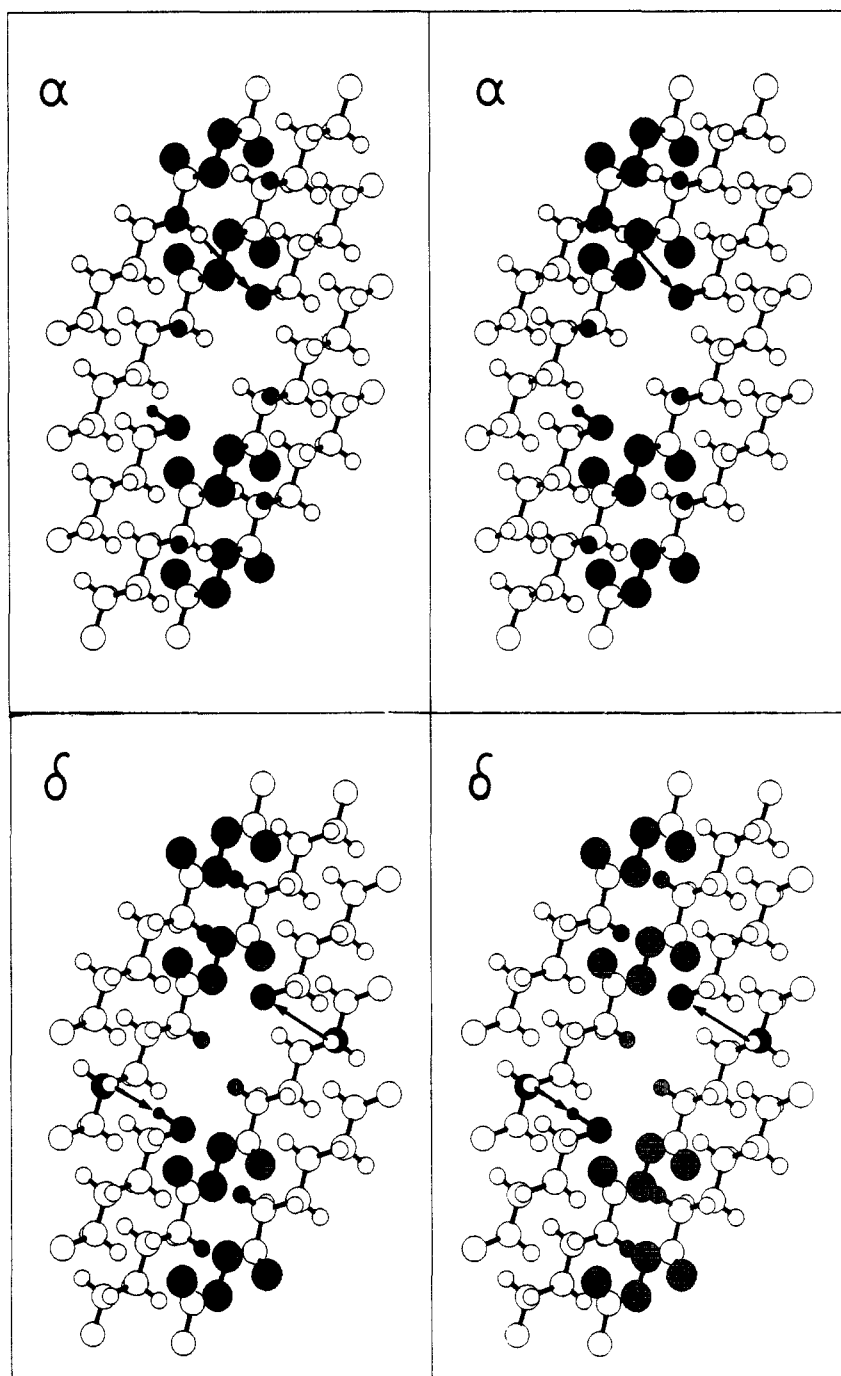


Figure 2. Stereopair plots of H transfer in crystalline BrUP viewed along $(\bar{1}10)$, the 2-fold rotation axis of intact molecules. (α) Space group $P4_32_12$; (δ) its enantiomorph, $P4_12_2$, related by reflection in the page. Geminal hydrogens, classed as axial or equatorial with respect to the dyad, exchange roles between space groups. The central molecule has lost two CO_2 's, and its radical carbons are shown without hydrogens as filled circles. The smaller filled circle indicates motion in the primary radical pair.^{1,2} Large shaded circles denote oxygen atoms of intact molecules; small shaded circles, their *pro-S* α -hydrogens. Arrows show H transfers that are observed when the shaded hydrogens are replaced by deuterium. Carbons that donate hydrogen and become radical centers are shown by filled circles. The radical-radical vector in pair- α is nearly vertical (110); that in pair- δ is nearly horizontal (001).

Individual $P4_12_2$ crystals were too small for EPR study, but prolonged photolysis of two crystals mounted together gave the spectrum of pair- δ upon annealing to 190 K (Figure 1f).¹⁴

Our recrystallizations seemed to give only one enantiomorphic space group or the other, perhaps because of intentional or adventitious seeding, but it is easy to imagine that a single crystallization could yield both crystal forms. In that case two crystals of the same substance, grown simultaneously from the same solution, and indistinguishable by routine X-ray diffraction, would follow completely different reaction paths, one beginning with

α -hydrogen abstraction, the other with δ -abstraction. In fact these crystals would be diastereomeric, one source of chirality being configuration at the deuterated carbon and the other being handedness of the crystal packing.

This work provides a clear example of a chiral crystal controlling stereo- and regiochemistry much as an enzyme would.¹⁵

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(13) Seeds were trimmed from the periphery of a "relay" crystal of the appropriately labeled compound grown with seeds from a differently labeled BrTP crystal whose configuration had been determined by X-ray and optical rotation. Relay assured isotopic purity of the final crystal.

(14) Other work showed that pair- δ is stable up to 235 K.

(15) For other examples of lattice-induced specificity, see: Green, B. S.; Arad-Yellin, R.; Cohen, M. D. *Top. Stereochem.* **1986**, *16*, 131-218. Desiraju, G. R., Ed. *Organic Solid State Chemistry*; Elsevier: Amsterdam, 1987.