Stereospecific γ-ray-induced dimerization of crystalline bis(*trans*-but-2-enoato)calcium

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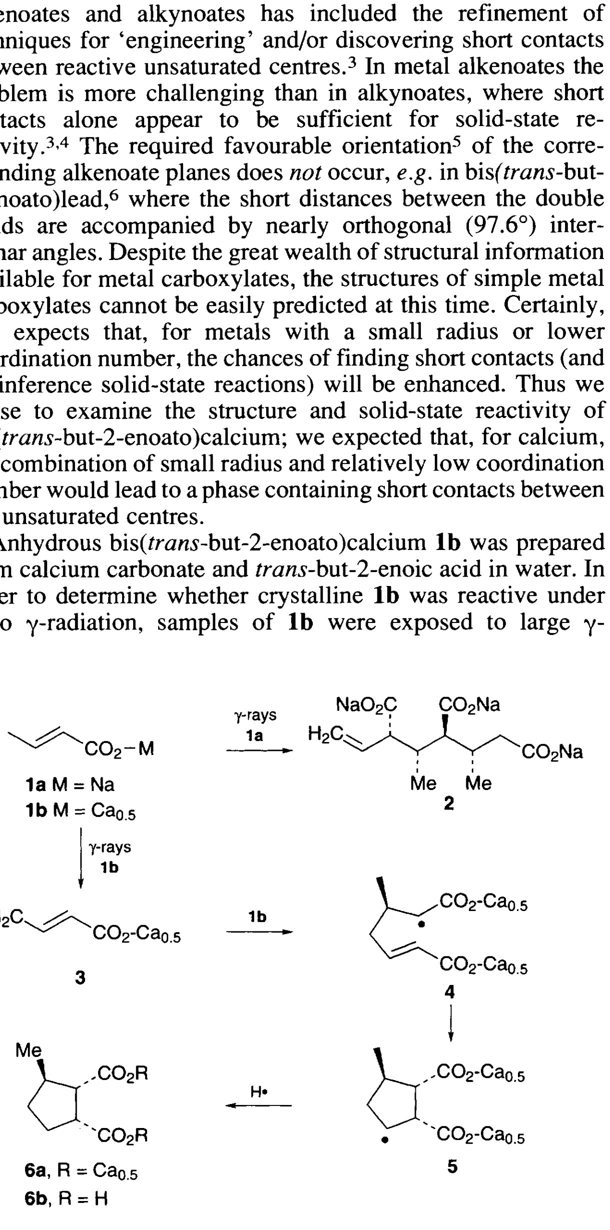
Irradiation (^{60}Co γ-rays) of crystalline bis(*trans*-but-2-enoato)calcium induces a unique solid-state cyclodimerization reaction; the product, *cis,trans*-nepetic acid, is one of four possible diastereomers.

Upon exposure to ^{60}Co γ-rays, metal complexes and salts containing α,β-unsaturated carboxylates exhibit extraordinary solid-state reactivity. Examples include the γ-ray-induced stereospecific trimerization of sodium *trans*-but-2-enoate **1a** to give **2**[1] and the regiospecific oxidation of *trans*-pent-2-enoate salts.[2] Our search for new solid-state reactions involving metal alkenoates and alkynoates has included the refinement of techniques for 'engineering' and/or discovering short contacts between reactive unsaturated centres.[3] In metal alkenoates the problem is more challenging than in alkynoates, where short contacts alone appear to be sufficient for solid-state reactivity.[3,4] The required favourable orientation[5] of the corresponding alkenoate planes does *not* occur, *e.g.* in bis(*trans*-but-2-enoato)lead,[6] where the short distances between the double bonds are accompanied by nearly orthogonal (97.6°) interplanar angles. Despite the great wealth of structural information available for metal carboxylates, the structures of simple metal carboxylates cannot be easily predicted at this time. Certainly, one expects that, for metals with a small radius or lower coordination number, the chances of finding short contacts (and by inference solid-state reactions) will be enhanced. Thus we chose to examine the structure and solid-state reactivity of bis(*trans*-but-2-enoato)calcium; we expected that, for calcium, the combination of small radius and relatively low coordination number would lead to a phase containing short contacts between the unsaturated centres.

Anhydrous bis(*trans*-but-2-enoato)calcium **1b** was prepared from calcium carbonate and *trans*-but-2-enoic acid in water. In order to determine whether crystalline **1b** was reactive under ^{60}Co γ-radiation, samples of **1b** were exposed to large γ-ray doses (*ca.* 90 Mrad) in a Gammacell 220 irradiator. The initial indication that reaction occurred was the water insolubility of a small portion of the product. The NMR spectrum of the water-insoluble calcium salt **6a** as the free acid **6b** in D_2O–DCl showed the presence of a single dimer: ^{1}H NMR δ 3.29 (ddd, 1, *J* 9.2, 8.1, 7.6 Hz), 2.72 (dd, 1, *J* 9.1, 8.1 Hz), 2.31 (m, 1), 1.96 (m, 3), 1.30 (m, 1), 1.08 (d, 3, *J* 6.7 Hz); ^{13}C NMR δ 178.9 (C), 178.5 (C), 53.8 (CH), 46.9 (CH) 37.8 (CH), 33.0 (CH), 28.2 (CH_2), 19.3 (CH_3). These data suggested that the dimer was a nepetic acid,[7] and the structure was established as *cis, trans*-nepetic acid (**6b**) by the identity of the ^{1}H and ^{13}C NMR spectra with those of an authentic sample kindly provided by Professor E. J. Eisenbraun of Oklahoma State University.



The unexpected formation of **6a** as the insoluble calcium salt prompted a more detailed examination of this reaction. Optimal conversion to product was obtained by two cycles of ^{60}Co γ-irradiation (2 × 0.7 Mrad) followed by heating at 60 °C for 24 h.† Dissolution in H_2O and filtration gave about 5% of the solid calcium salt **6a**. Since we anticipated that other water-soluble products were formed, the entire irradiated material was analysed as the free acid by ^{1}H NMR spectroscopy in D_2O–DCl and the free-acid mixture was converted to methyl esters with diazomethane for analysis by ^{1}H NMR spectroscopy and GC. GC and GC/MS analysis of the methyl esters indicated that the irradiation/heating cycles had produced 10% conversion to a 76:3:6:15 mixture of **6**, two other dimers and a trimer. The differences in mass spectral fragmentation patterns established that the other two dimers are not stereoisomers of **6**. The NMR spectral data of the mixture also indicated 10% conversion to products. The NMR spectrum of the methyl esters showed a small peak at δ 6.92 (dd, 1, *J* 15.7, 7.5 Hz) which is probably due to a $-CH_2CH{=}CHCO_2Me$ group in the trimer. The minor amounts of the three other products preclude more complete characterization.

The cyclodimerization process providing **6a** exhibits several remarkable characteristics. Recovered bis(*trans*-but-2-enoato)-calcium may be recrystallized and recycled; thus, the reaction is an efficient, chemo- and stereo-specific, solid-state synthesis of a small molecule using ionizing radiation.[8] Another rare example is the radiation-induced trimerization of sodium *trans*-but-2-enoate to give **2**.[1] Cyclodimerization of *trans*-but-2-enoate in solution or in the solid state is unprecedented. Even more striking is the formation of the nepetic acid **6** in 76% yield at 10% conversion as only one of four possible diastereoisomers. Dimerizations of α,β-unsaturated carbonyl compounds typically lead to acyclic molecules[9] or [2 + 2] cycloadducts photochemically.[10]

In order to establish whether the intermolecular orientation and distances suggest that topochemical effects might be responsible for at least the onset of solid-state reactivity,[11] we performed an X-ray structure determination on single crystals of **1b**.‡ The crystal structure of **1b** consists of two-dimensional octahedral calcium coordination polymers in crystal *bc* planes; the dihedral angle between adjacent pairs of butenoate planes in this structure is 14.4°. Fig. 1 shows the octahedral coordination environment of a single calcium ion; each Ca^{2+} ion occupies a site of crystallographic C_2 symmetry. Short contacts arise

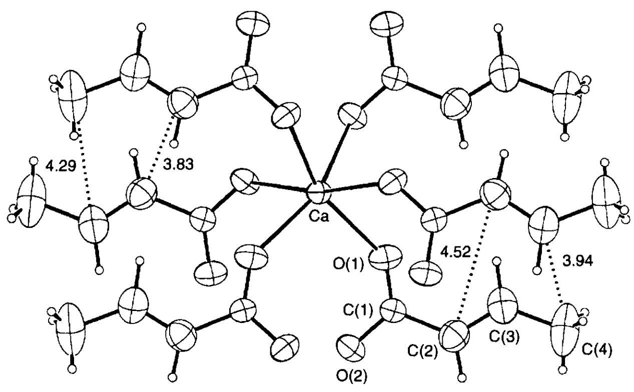


Fig. 1 View of a single calcium ion, showing the octahedral coordination and important short C···C contacts between butenoate moieties in **1b**

between pairs of but-2-enoate moieties coordinated to a single calcium ion; the shortest contacts are shown in Fig. 1. Inspection suggests that if a reaction were to occur between either pair of molecules shown, a nepetate with *trans*-carboxylate groups would be produced. Thus, we must look more carefully at Fig. 1 in a mechanistic context. The shortest distance, 3.83 Å, occurs between two α-carbon atoms; bond formation between these two atoms as a first step precludes a final product with *cis*-carboxylate groups. Using the 3.94 Å contact, the initial step would involve addition of allyl radical **3** (formed by γ-ray induced loss of a hydrogen atom from **1b**) to the β-carbon atom of a second butenoate **1b** to give radical **4**. In the restricted crystal environment, bond rotation could occur to bring the radical to a position where 5-*endo* cyclization[12] to give cyclopentyl radical **5** can take place. Hydrogen abstraction, possibly from another molecule of **1b**, would generate **6a**.

Most radiation-induced solid-state oligomerization reactions lead to products accompanied by little detectable stereochemical control.[13] However, as we have pointed out previously,[1] the stereospecific trimerization of **1a** may represent the earliest steps in a solid-state polymerization process.§ The cyclodimerization of **1b**, again proceeding with strong stereochemical control, demonstrates that studies of radiation-induced processes in metal alkenoates provide an excellent opportunity for the development, discovery and understanding of unique new stereospecific syntheses. Such studies, currently underway in out laboratories, promise to clarify the relationship between ground-state crystal structure and product stereochemistry in radiation-induced solid-state reactions.

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Footnotes

† No detectable product is formed when **1b** is not irradiated but is only heated at 60 °C for 24 h.

‡ *Crystal data* for **1b**: $C_8H_{10}CaO_4$, M = 210.24, monoclinic, space group $P2/c$, a = 14.795(7), b = 5.229(3), c = 6.443(3) Å, β = 104.73(5)°; $Z=2$; U = 482.1(8) Å^3; D_m = 1.42(2) g cm^{-3}, D_c = 1.448 g cm^{-3}; crystal dimensions 0.13 × 0.21 × 0.42 mm; T = 294 K. Data were collected to a maximum 2θ = 50° [λ(Mo-Kα) = 0.71073 Å], using ω scans; no absorption corrections were made. Full-matrix least-squares refinement (based on $|F|$) of positional and anisotropic displacement parameters for all nonhydrogen atoms, and isotropic displacement parameters for H atoms, with fixed, restrained methyl H atoms, (total parameters = 68) led to R = 0.061 and R_w = 0.063, using 656 data for which $I > 1.96\sigma(I)$ [R = 0.101 for all 845 reflections; maximum residual ρ = 0.63 e Å^{-3}]. Programs used: ORTEP, CRYSTALS.[14] Atomic coordinates, bond lengths and angles, and thermal displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/72.

§In the early stages of methacrylate polymerization, stereoregular triads were observed.[13b]

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