

nonreactivity of the methylene hydrogens of **1c** toward abstraction indicates that stabilization of the 1,6-diradical **5** is necessary for the 1,5-hydrogen transfer.

Much attention has recently been given to investigations on diradicals.¹² 1,6-Diradicals have been generated by 1,7-hydrogen transfer (vide supra) or Norrish type I reaction (α -cleavage) of cyclohexanones.¹³ The results of the present reactions indicate that 1,5-hydrogen transfer of 1,2-disubstituted alkenes becomes possible when the hydrogens are strongly activated by substituents. This kind of photoreaction provides a novel entry to the 1,6-diradicals.

(12) For recent reviews, see: (a) Wilson, R. M. *Org. Photochem.* 1985, 7, 339. (b) Borden, W. T. Ed. *Diradicals*; Wiley: New York, 1982. (13) (a) Weiss, D. S. *Org. Photochem.* 1981, 5, 347. (b) Caldwell, R. A.; Sakuragi, H.; Majima, T. *J. Am. Chem. Soc.* 1984, 106, 2471.

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Received June 9, 1987

Crystal Engineering a Solid-State Diels-Alder Reaction

Summary: [3,4-(Methylenedioxy)phenyl]propionic acid was predicted to and does in fact crystallize with a short axis of 4 Å and with a packing such that diene and dienophile components in adjacent molecules may participate in an intermolecular solid-state Diels-Alder reaction.

Sir: Crystal engineering is concerned with the predictive design of topochemical processes, by understanding the nature of weak yet directionally specific nonbonded forces.¹ Here, we describe such a deliberately "engineered" intermolecular solid-state Diels-Alder reaction which seems quite general and may offer considerable scope for a more systematic chemistry of molecular solids.

The strategy involved identification of a substance which may act as either diene or dienophile and further crystallize in a structure which permits a topochemical 4 + 2 conversion. Accordingly, substituted phenylpropionic acids were considered; not only are they used in self-Diels-Alder reactions in lignan synthesis^{2,3} but the crystallography of the structurally related *trans*-cinnamic acids has been extensively investigated.^{4,5}

(1) Schmidt, G. M. J. *Pure Appl. Chem.* 1971, 27, 647. Leiserowitz, L.; Schmidt, G. M. J. *J. Chem. Soc. A* 1969, 2372. Alcock, N. W.; Herron, N.; Kemp, T. J.; Shoppee, C. W. *J. Chem. Soc., Chem. Commun.* 1975, 785. Thomas, N. W.; Ramdas, S.; Thomas, J. M.; *Proc. R. Soc. London, A* 1985, 400, 219. Desiraju, G. R. *Endeavour* 1984, 8, 201. Desiraju, G. R.; Sarma, J. A. R. P. *J. Chem. Soc., Chem. Commun.* 1983, 45. Sarma, J. A. R. P.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* 1984, 145. Sarma, J. A. R. P.; Desiraju, G. R. *J. Am. Chem. Soc.* 1986, 108, 2791.

(2) Haworth, R. D.; Kelly, W. *J. Chem. Soc.* 1936, 745.

(3) Ward, R. S. *Chem. Soc. Rev.* 1982, 11, 75. Holmes, T. L.; Stevenson, R. J. *Org. Chem.* 1971, 36, 3450. Brown, D.; Stevenson, R. *J. Org. Chem.* 1965, 30, 1759. Brown, D.; Stevenson, R. *Tetrahedron Lett.* 1964, 3213.

(4) Schmidt, G. M. J. *J. Chem. Soc.* 1964, 2014. Bryan, R. F.; Freyberg, D. P. *J. Chem. Soc., Perkin Trans. 2* 1975, 1835.

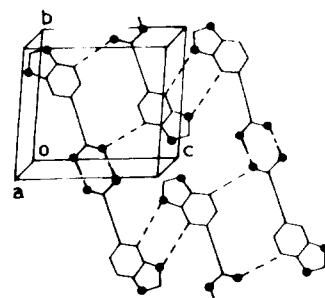


Figure 1. View of the crystal structure of [3,4-(methylenedioxy)phenyl]propionic acid (**2**) down the 4-Å short axis. The molecular sheets lie parallel to (111). O-H...O and C-H...O bonds are indicated.

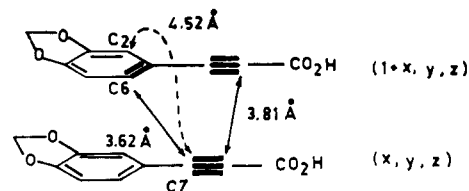
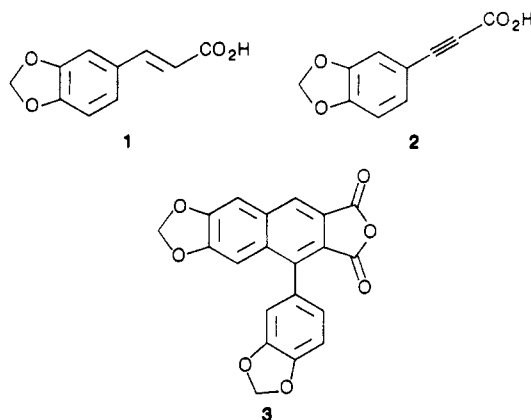


Figure 2. Schematic view of a topochemical Diels-Alder reaction for acid **2**.

The methylenedioxy substituent may "steer" the crystal structure of a planar aromatic to the 4-Å short axis structure (β structure) because of in-plane C-H...O interactions which stabilize the formation of two-dimensional molecular motifs.^{5,6} In 3,4-(methylenedioxy)cinnamic acid (**1**), for instance, these motifs are planar sheets, stacking of which leads to the 4-Å axis. Additionally, other factors



being constant, a planar aromatic having a higher C/H stoichiometric ratio prefers the β and related structures with overlapping, stacked molecules.⁷ So, 1,4-diethylnaphthalene, $C_{14}H_{10}$, adopts the β structure,⁸ while naphthalene, $C_{10}H_8$, with a lower C/H ratio, does not. Analogously, one may extrapolate from the β structure of **1**, $C_{10}H_8O_4$, that of [3,4-(methylenedioxy)phenyl]propionic acid (**2**), $C_{10}H_8O_4$. Both **1** and **2** are planar molecules with similar volumes, shapes, and functionalities. The smaller number of hydrogen atoms in **2** was expected, in fact, to enhance the tendency for β structure adoption.

This prediction was confirmed in its crystal structure analysis.⁹ Figure 1 shows that molecules of **2** form a

(5) Desiraju, G. R.; Kamala, R.; Kumari, B. H.; Sarma, J. A. R. P. *J. Chem. Soc., Perkin Trans. 2* 1984, 181.

(6) Sarma, J. A. R. P.; Desiraju, G. R. *Acc. Chem. Res.* 1986, 19, 222.

(7) Desiraju, G. R.; Gavezzotti, A., submitted for publication in *Acc. Chem. Res.*

(8) Enkelmann, V.; Rohde, O. *Acta Crystallogr., Sect. B* 1977, B33, 3531.

compact sheet characterized by O-H...O (O...O, 2.63 Å) and C-H...O (C...O, 3.36, 3.39 Å) bonds. These contacts stabilize the sheet motif and with it the β structure. The chemical consequences of this crystal structure are revealed in the thermal decomposition of solid **2**. While the reported "melting point" is 165 °C, we find that anhydride **3**, the Diels-Alder product, is formed at even 70 °C, the solid turning yellow-brown. Sublimation and decarboxylation account for some loss of material.¹¹

Inspection of Figure 2 shows the orientation of the "incipient" reactive centers. The triple bond in the reference molecule is the dienophile, while the conjugated triple bond in the short axis translated neighbor is the diene. This arrangement closely parallels Haworth's original synthesis of **3**, where **2** is refluxed with C_2O , forming its anhydride and thereby bringing diene and dienophile to within reacting distance. In the solid state, this is successfully effected by the crystal structure itself. To give **3**, the initial 4 + 2 reaction must be followed by a secondary hydrogen shift from the allenic intermediate and also by loss of water. There is much precedent for similar processes in the solid state.¹²

We infer, as follows, that this reaction is a genuine solid state topochemical process and not a result of partial melting: (a) reaction occurs easily below 120 °C, an approximately 25% conversion to **3** occurring in 30 days at 120 °C or 50 days at 90 °C; (b) the mixture remains free-flowing without any signs of melting; (c) X-ray powder traces of the mixture may be recorded at various stages of conversion; (d) crystalline phenylpropionic acid, $\text{C}_6\text{H}_5\text{-C}\equiv\text{CCO}_2\text{H}$, which does not have a β structure¹³ is unaffected by heating yet is converted into its Diels-Alder anhydride if refluxed with Ac_2O ; (e) a year-old sample of **2** stored under ambient conditions (maximum temperature 43 °C) showed definite changes in color and X-ray diffractograms.

The reaction is also quite general. The 4-chloro (short axis 3.962 Å), 3,4-dimethoxy (3.891 Å), and 3,4,5-trimethoxy (3.942 Å) derivatives all adopt β structures and all react similarly when heated, the trimethoxy compound reacting relatively rapidly.¹⁴ Invariably the reaction temperature is 50-100 deg below the reported "melting point". With the unsubstituted compound (5.1 Å) being unreactive and the 4-methoxy (8.96 Å) compound also unreactive, an analogy to the α -, β -, and γ -cinnamic acids seems appealing.⁴ However, we defer such a classification till we examine related acids for many of which variable melting points have been reported.¹⁵ Such variations are heating-rate dependent and seem to be good pointers to solid-state reactivity. In general, any crystalline phenylpropionic acid may be expected to form Diels-Alder products upon heating if the triple bonds are sufficiently close for topochemical reaction.

(9) Acid **2**: $P\bar{1}$, $Z = 2$, $a = 3.807$ Å, $b = 10.297$ Å, $c = 10.995$ Å, $\alpha = 84.07^\circ$, $\beta = 96.46^\circ$, $\gamma = 98.13^\circ$, CAD-4 (RSIC, IIT Madras), $\text{Mo K}\alpha$, 746 3 σ reflections out of 1219 with $3^\circ \leq \theta \leq 28^\circ$, MULTAN-80, SHELX-76, $R = 0.056$, $R_w = 0.057$, hydrogens isotropic.

(10) Baude, S.; Reychler, A. *Bull. Soc. Chim. Fr.* 1897, 17, 616.

(11) Typically 200 mg of **2** were heated at 120 °C for 5 weeks. TLC separation (Silica gel, 15% EtOAc-hexane) gave [3,4-(methylenedioxy)-phenyl]acetylene (63 mg), unreacted **2** (20 mg) and anhydride **3** (44 mg). The IR, NMR, and MS of **3** matched those of an authentic sample.

(12) Scheffer, J. R. *Acc. Chem. Res.* 1980, 13, 283. Lewis, T. W.; Duesler, E. N.; Kress, R. B.; Curtin, D. Y.; Paul, I. C. *J. Am. Chem. Soc.* 1980, 102, 4659. Lamartine, R.; Perrin, R.; Vicens, J.; Gamet, D.; Perrin, M.; Oehler, D.; Thozet, A. *Mol. Cryst. Liq. Cryst.* 1986, 134, 219.

(13) Rollett, J. S. *Acta Crystallogr.* 1955, 8, 487.

(14) Desiraju, G. R.; Kishan, K. V. R.; Murty, B. N., unpublished work.

(15) There are at least 10 such phenylpropionic acids. 2-Nitro: Schofield, K.; Simpson, J. C. E. *J. Chem. Soc.* 1945, 512. 4-Chloro and 4-nitro: Newman M. S.; Merrill, S. H. *J. Am. Chem. Soc.* 1955, 77, 5549. 3-Methyl: Benghiat, I.; Becker, E. I. *J. Org. Chem.* 1958, 23, 885.

The behavior of **2** appears to be representative of a new class of solid-state reactions which may not only be deliberately engineered but also be of considerable interest in lignan biosynthesis.

Acknowledgment. We thank the DST(SERC) for financial support.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters and intramolecular geometrical calculations (2 pages). Ordering information is given on any current masthead page.

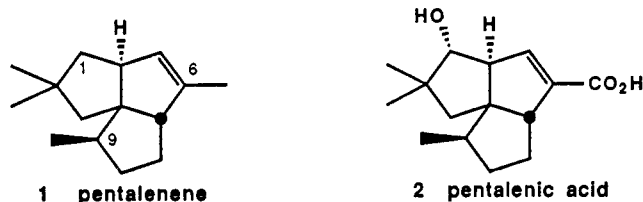
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Stereocontrolled Total Synthesis of Pentalenenes via [2 + 3] and [4 + 1] Cyclopentene Annulation Methodologies

Summary: Pentalenene and epipentalenene have each been prepared from enone **5** via [2 + 3] cyclopentene annulation in eight steps. A brief investigation of unexpected diradical cleavage of several vinylcyclopropanes was undertaken. The synthesis has been compared to a previous preparation of title compounds via [4 + 1] cyclopentene annulation in 14 steps.

Sir: Pentalenene (**1**) and pentalenic acid (**2**) belong to the class of sesquiterpenes classified as nonlinearly fused triquinanes.² These closely related compounds have been



isolated from the broth of *Streptomyces griseochromogens*³ and their role in the biogenesis of the antibiotic pentalenolactone has been actively investigated.⁴ Equally active has been the effort in the area of total synthesis where the title compounds represent attractive targets.⁵

(1) Fellow of the Alfred P. Sloan Foundation, 1981-1985; Recipient of the NIH Research Career Development Award, 1984-1989.

(2) Paquette, L. A. *Top. Curr. Chem.* 1984, 119, 1.

(3) Isolation. (i) Pentalenene: Seto, H.; Yonehara, H. *J. Antibiot.* 1980, 33, 92. (ii) Pentalenic acid: Seto, H.; Sasaki, T.; Uzawa, J.; Takeuchi, S.; Yonehara, H. *Tetrahedron Lett.* 1978, 4411.

(4) (a) Cane, D. E.; Tillman, A. M. *J. Am. Chem. Soc.* 1983, 105, 122. (b) Cane, D. E.; Rossi, T.; Tillman, A. M.; Pachlatko, J. P. *J. Am. Chem. Soc.* 1981, 103, 1838.

(5) Synthesis. (i) Pentalenene: (a) Ohfuné, Y.; Sirahama, H.; Matsumoto, T. *Tetrahedron Lett.* 1976, 2869. (b) Misumi, S.; Ohtsuka, T.; Ohfuné, Y.; Sugita, K.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* 1979, 31. (c) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* 1982, 104, 4504. (d) Paquette, L. A.; Annis, G. D. *J. Am. Chem. Soc.* 1983, 105, 7358. (e) Piers, E.; Karunaratne, V. J. *Chem. Soc., Chem. Commun.* 1984, 959.

(f) Pattenden, G.; Teague, S. J. *Tetrahedron Lett.* 1984, 3021. (g) Mehta, G.; Rao, K. S. *J. Chem. Soc., Chem. Commun.* 1985, 1464. (h) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* 1986, 108, 800. (i) Hua, D. H. *J. Am. Chem. Soc.* 1986, 108, 3836. (j) Imanishi, T.; Ninbari, F.; Yamashita, M.; Iwata, C. *Chem. Pharm. Bull.* 1986, 34, 2268. (k) Mehta, G.; Rao, K. S. *J. Am. Chem. Soc.* 1986, 108, 8015. (ii) Pentalenic acid: (l) Sakai, K.; Ohtsuka, T.; Misumi, S.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* 1981, 355. (m) Crimmins, M. T.; DeLoach, J. A. *J. Org. Chem.* 1984, 49, 2076. (n) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* 1986, 108, 800.