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Crystal Chemistry of Some (Alkoxyphenyl)propiolic Acids. The Role of Oxygen and Hydrogen Atoms in Determining Stack Structures of Planar Aromatic Compounds[†]

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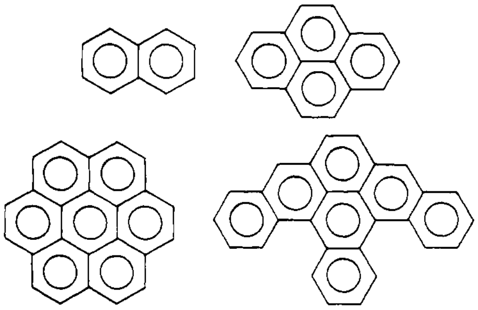
Abstract: Crystal structures of planar oxygenated aromatic compounds are determined by an interplay of C···H interactions which steer to herringbone structures, characterized by adjacent inclined molecules, and C–H···O interactions, which being lateral, steer to stacked-sheet structures with short axes of 3.8–4.2 Å. The number of hydrogen and oxygen atoms in the molecule seems to determine which of these two preferences is exercised, a smaller number of hydrogens and a greater number of oxygens leading to the stack structure. Accordingly, if an alkoxycinnamic acid has a stack structure, the corresponding phenylpropiolic acid will, in all likelihood, have the same structure. This is exemplified by the pair of nearly isomorphous compounds 3,4-(methylenedioxy)cinnamic acid and [3,4-(methylenedioxy)phenyl]propiolic acid. The structure of the latter is triclinic, $P\bar{1}$, $Z = 2$, $a = 3.807$ (2) Å, $b = 10.297$ (2) Å, $c = 10.995$ (3) Å, $\alpha = 84.07$ (2)°, $\beta = 96.46$ (3)°, $\gamma = 98.13$ (3)°. Even if a cinnamic acid does not have a 4-Å structure, the removal of two hydrogen atoms to give the propiolic acid could result in the stack structure for the latter. Accordingly, (3,4-dimethoxyphenyl)propiolic acid is triclinic, $P\bar{1}$, $Z = 2$, $a = 3.891$ (1) Å, $b = 11.361$ (3) Å, $c = 12.089$ (4) Å, $\alpha = 112.50$ (2)°, $\beta = 92.53$ (3)°, $\gamma = 96.12$ (3)°. A large number of oxygen atoms acting as C–H···O bond acceptors can lead to a stack structure for significantly nonplanar molecules. An example is (3,4,5-trimethoxyphenyl)propiolic acid which is monoclinic, $P2_1/n$, $Z = 4$, $a = 20.806$ (6) Å, $b = 14.159$ (3) Å, $c = 3.942$ (5) Å, $\beta = 94.79$ (7)°. In contrast, (4-methoxyphenyl)propiolic acid, which does not have the critical number of oxygen atoms, does not have a 4-Å stack structure being triclinic, $P\bar{1}$, $Z = 2$, with $a = 10.767$ (3) Å, $b = 8.494$ (3) Å, $c = 7.499$ (2) Å, $\alpha = 99.01$ (2)°, $\beta = 125.62$ (2)°, $\gamma = 112.42$ (2)°. The crystal structures of these and other phenylpropiolic acids are closely paralleled by their solid-state thermal reactivities. Acids with a 4-Å stack structure participate in an intermolecular Diels–Alder reaction to give derivatives of 1-phenylnaphthalene-2,3-dicarboxylic acid anhydride, while those with short axes greater than 4.2 Å are unreactive. The products of these reactions may be rationalized by assuming that adjacent double and triple bonds, within a threshold distance of ca. 4.5 Å in the crystal, are potentially reactive. In general, any crystalline phenylpropiolic acid may be expected to form Diels–Alder products upon heating if the triple bonds are sufficiently close for topochemical reaction. The formation of these lignan derivatives from acetylenic precursors under mild conditions could be of biosynthetic significance.

A survey of the crystallographic literature shows that aromatic rings pack in two fundamentally different ways.[1] The first is the so-called herringbone pattern, where adjacent rings are inclined at steep angles (50–90°) with the hydrogen atoms of one ring pointing toward the carbon atoms of the other. It has been suggested that the herringbone pattern is stabilized by C(δ–)···H(δ+) interactions.[2] The second pattern is the C···C stabilized stack structure, where adjacent molecules are parallel and highly overlapped. These patterns are found in isolation or together in a wide variety of crystals ranging from simple aromatic hydrocarbons to globular proteins and they represent the only ways in which aromatic rings can pack in crystals. These observations on herringbone and stack structures are confirmed by ab initio calculations[3] and molecular beam studies of van der Waals complexes.[4] We have shown previously that oxygen atoms on the periphery of a planar aromatic hydrocarbon exert a significant effect in steering from a herringbone to a stack structure through the formation of weak C–H···O hydrogen bonds.[5,6] In this paper, we show that this effect may be analyzed in terms of a reduction in the number of peripheral hydrogen atoms which tend to form herringbone-directing C···H contacts. These ideas have been used in the design of a family of crystal structures, the alkoxy-substituted phenylpropiolic acids, that exhibit an unusual solid-state transformation, an intermolecular Diels–Alder reaction.[7] It is interesting to note that hardly anything has been reported previously concerning the solid-state chemistry of these simple compounds.

Results and Discussion

Aromatic-Packing Modes and C:H Stoichiometric Ratios.



Planar aromatic hydrocarbons adopt one of four basic structural types exemplified by naphthalene, coronene, pyrene, and tribenzopyrene (Figure 1; see also panel below). These structure types are defined by the short crystallographic axis and the angle between the mean planes of the nearest adjacent molecules. Crystals with the naphthalene structure are stabilized largely by C···H interactions and are characterized by the herringbone pattern

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[†] Dedicated to Prof. D. Y. Curtin on the occasion of his 68th birthday.

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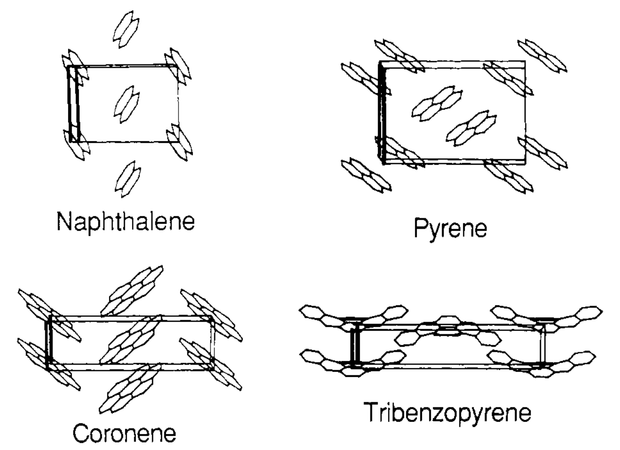

Figure 1. The four basic aromatic crystal packings. The short axes are indicated in each case.

with short axes in the range 5.2–6.9 Å. Adjacent molecules are inclined at intermediate angles in the range 40–60°. The tribenzopyrene structure, also termed the β-structure,[5,8] is a pure C···C-stabilized stack and has short axes in the range 3.8–4.2 Å. The coronene and pyrene structures are more complex since they contain both herringbone and stack motifs. In the former, molecules are stacked with a crystallographic repeat between 4.7 and 5.0 Å, but the stacks themselves are related in a herringbone fashion with adjacent molecules making steep angles between 80° and 90°. In the latter, the basic motif is a stacked diad which is repeated with the herringbone pattern. The short axis in this structure is in the range 7.5–8.5 Å.

The adoption of one or another of these structure types by a pure aromatic hydrocarbon, i.e., one without any substituents and having only sp^2 carbon atoms, may be understood by a consideration of the positioning and number of hydrogen atoms in the molecule, especially relative to the number of carbon atoms. In general, the importance of hydrogen atoms in determining stable packings of organic molecules must be stressed. These atoms are situated at the molecular periphery and play a crucial role in defining molecular shape. Therefore they are of the utmost importance in close packing. As early as 1965, Craig et al. have stated that crystal structures of close-packed solids may be determined by a consideration of hydrogen atom repulsions alone.[9] The validity of this statement accounts for the many successes in determining crystal structures with packing calculations.[10] A study of a large number of crystal structures of condensed aromatic hydrocarbons shows further that C···H interactions are optimized in crystal packing in preference to C···C and H···H interactions. The reason for this preference is unclear but could be related to the slight electrostatic character of the C···H interaction as compared to the H···H and C···C interactions. The crystallographic consequences are, however, unequivocal for condensed aromatic hydrocarbons. If such a molecule is planar, C···H interactions are always important and the structure adopted is either the naphthalene-, coronene-, or pyrene-type, depending on the C:H stoichiometric ratio. If this ratio is low (typically <1.50), the naphthalene structure is obtained. If the ratio is somewhat higher (typically >1.50), C···C interactions also become important and either the coronene or pyrene structure is obtained. It is significant that planar aromatic hydrocarbons without substituents and containing only sp^2 carbons never adopt crystal packings stabilized by C···C and H···H interactions in the absence of C···H interactions. A preference for such a structure could, however, be manifested at C:H ratios lower than 1.00. Such a ratio is not possible for a pure aromatic since the minimum value is 1.00 for benzene. But hexamethylbenzene (C:H 0.67) adopts a stack structure characterized by C···C and gear-mesh H···H interactions.[11]

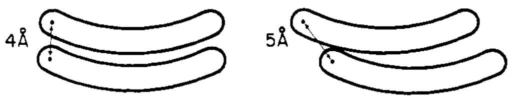

Figure 2. Schematic diagram to show why a bow-shaped molecule cannot crystallize with a short axis much greater than 4 Å if it adopts a stack structure. The molecular plane is perpendicular to the plane of the paper. Notice the bad contact in the 5-Å structure.

The pure stack or β-structure is also observed at high C:H ratios (for instance in tribenzopyrene[12]) if the molecular shape is bowed rather than planar. Absence of C···H interactions is probably because the adoption of the coronene structure, which is the alternative packing mode for a high C:H compound, is difficult for markedly nonplanar molecules (Figure 2). Even when adopted by bow-shaped molecules, the molecular stacks in the tribenzopyrene structure are not held together very efficiently. So weak are the lateral H···H interactions that many of these crystals are disordered or are modulated in directions perpendicular to the stack.[13]

In contrast to hydrocarbons, their heteroatom derivatives show a pronounced tendency to adopt the stacked β-structure.[5] This is true for both planar and nonplanar molecules. We have previously analyzed the role of heteroatoms such as O, Cl, Br, and S in the adoption of stack structures with short axes of 3.8–4.2 Å.[5,6,14,15] These heteroatoms are involved in short directional contacts such as C–H···O, Cl···Cl, Br···Br, S···Cl, and S···S, which being lateral can serve in organizing the molecules into two-dimensional motifs such as sheets or ribbons. Stacking of these motifs is the only possible way of completing the three-dimensional structure. Since a direct overlap of atom on atom is energetically unfavorable, there is a slight lateral offset between layers leading to a short axis of around 4.0 Å. It is convenient then to view the crystal structure of a heteroatom-substituted planar aromatic compound in terms of a competition between interactions which would lead to either stack (heteroatom contacts) or herringbone (C···H) motifs.

C:H:O Ratios and Crystal Engineering of Stack Structures. Oxygen atoms pendant on an aromatic moiety either as substituents or as heterocyclic replacements for carbon atoms may form C–H···O hydrogen bonds which lead to stack-structure adoption.[5,6] Such oxygen atoms significantly favor the stack structure for three reasons: (1) they form lateral C–H···O contacts, (2) such contacts "tie up" some of the C–H hydrogen atoms which might otherwise be stabilized by herringbone-directing C···H contacts, and (3) they alter the C:H ratio as for instance when a >C=O group replaces a >C–H group. Factors 2 and 3 effectively raise C:H ratios and with it the tendency for a stack structure. The importance of C:H:O ratios in steering to stack structures has been demonstrated for a large number of quinones, furans, and other oxygenated aromatics.[5,6] To summarize, it may be stated that the stack structure is favored by higher C:H ratios and that these ratios are effectively raised by oxygen atoms.

It was felt that these ideas could be fruitfully applied in the design of crystal structures which would permit an intermolecular solid-state Diels–Alder reaction. The strategy involved identification of substances which may act as either diene or dienophile

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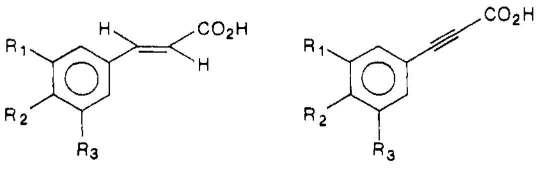

1 **2**

a: R_1, R_2 = -OCH_2O-; R_3 = H
b: R_1 = R_2 = CH_3O; R_3 = H
c: R_1 = R_2 = R_3 = CH_3O
d: R_1 = R_3 = H; R_2 = CH_3O
e: R_1 = R_2 = R_3 = H

and further crystallize in a structure which permits a topochemical 4 + 2 conversion. Accordingly, substituted phenylpropiolic acids were considered; not only are they used in self-Diels–Alder reactions in lignan synthesis[16] but the crystallographically related *trans*-cinnamic acids have been extensively investigated.[8,17] Further, many naturally occurring lignans contain phenyl rings substituted by groups such as 3,4-methylenedioxy, 3,4-dimethoxy and 3,4,5-trimethoxy.[16] The starting point in this crystal-engineering exercise, the 4-Å stack structure of 3,4-(methylenedioxy)cinnamic acid, **1a**, was therefore quite deliberately chosen. This crystal structure is layered, the layers being formed by a C–H···O linking of O–H···O=C bonded centrosymmetric dimers.[5,18a,b] As described above, other factors being constant, a planar aromatic having a higher C:H ratio prefers the stack structure. Accordingly, one may extrapolate from the β-structure of **1a**, $C_{10}H_8O_4$, that of [3,4-(methylenedioxy)phenyl]propiolic acid, $C_{10}H_6O_4$, **2a**. Both **1a** and **2a** 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 stack-structure adoption.

This prediction was confirmed in its crystal-structure analysis. Table I summarizes the crystallographic details for acids **2a–d**, the structures of which were determined in this study. Acids **1a**[18b] and **2a** have unit cells of nearly the same dimensions and space group, and the crystal packings are virtually identical. Figure 3 shows that molecules of **2a** form a compact sheet characterized by O–H···O (O···O 2.63 Å) and C–H···O (C···O 3.36, and 3.39 Å) bonds. These contacts stabilize the sheet motif and with it the stacked β-structure. It may be noted that the C–H···O interactions are specific enough to cause ordering of the carboxyl group.[19] The two C–O distances are 1.31 (1) and 1.23 (1) Å and the C–H···O bond involves the carbonyl oxygen rather than the carboxyl oxygen. Figure 3 shows that the approach of the C–H group toward the carbonyl oxygen is almost in the lone-pair direction.

In interesting contrast, the pair of acids 3,4-dimethoxycinnamic acid, **1b**, and (3,4-dimethoxyphenyl)propiolic acid, **2b**, have different crystal structures. While acid **1b**, $C_{11}H_{10}O_4$, has a layered structure,[18a,c] the layers are inversion rather than translation stacked, leading to a short axis of 8.4 Å. Acid **2b**, $C_{11}H_8O_4$, with two less hydrogen atoms, however, crosses the structural threshold into the 4-Å domain. Figure 4 shows that molecules are held compactly in layers which are stacked along the 4-Å direction. The layers are held by O–H···O (2.67 Å) and C–H···O (3.38, 3.53 Å) contacts, involving both methoxy and aromatic hydrogen atoms.

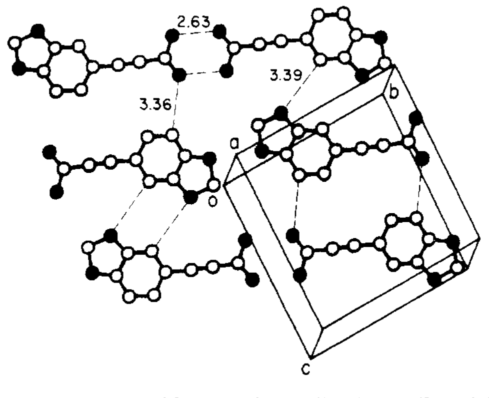

Figure 3. Layer structure of [3,4-(methylenedioxy)phenyl]propiolic acid, **2a**. Oxygen atoms are shaded. C–H···O and O–H···O bonds are indicated with dashed lines.

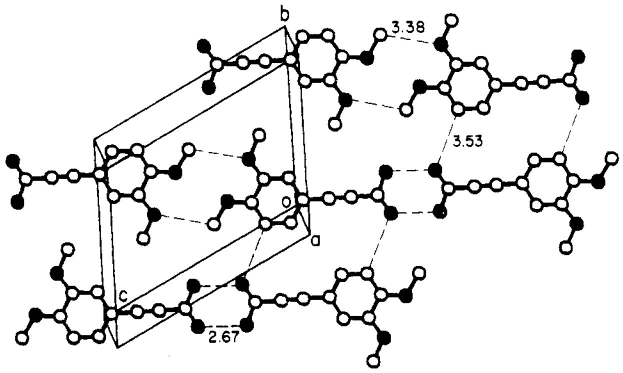

Figure 4. Layer structure of (3,4-dimethoxyphenyl)propiolic acid, **2b**.

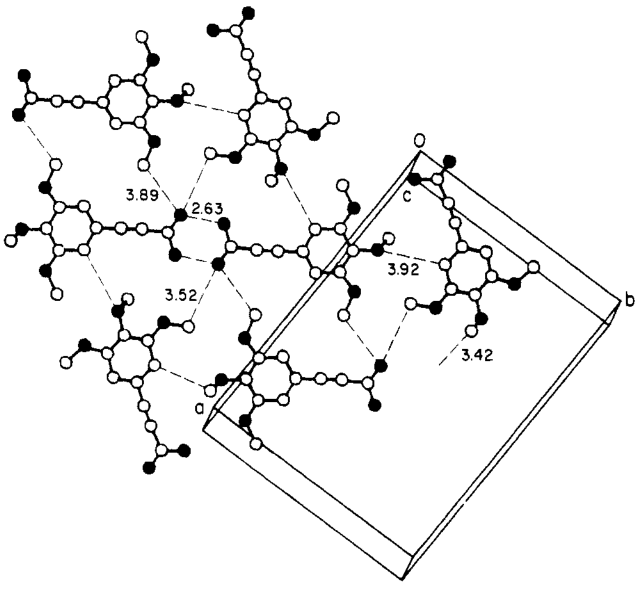

Figure 5. Layer structure of (3,4,5-trimethoxyphenyl)propiolic acid, **2c**. The internal methoxy group is bent out of the mean plane.

These C–H···O contacts are again sufficient to cause carboxyl-group ordering, the two C–O distances being 1.31 (1) and 1.22 (1) Å, with the carbonyl oxygen forming the 3.53-Å C–H···O contact.

The importance of C:H:O ratios in stack-structure adoption is further revealed in the 4-Å structure of (3,4,5-trimethoxyphenyl)propiolic acid, **2c**. While the crystal structure of the corresponding cinnamic acid, $C_{12}H_{14}O_5$, **1c**, is unknown, acid **2c**, $C_{12}H_{12}O_5$, is a rare example of a 4-Å stack structure for a compound with a 1,2,3-trimethoxyphenyl group. The 1988 Cambridge Database (69691 entries) has 100 entries with the 1,2,3-trimethoxy group; of these, only a solitary compound has a short axis in the

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Table I. Crystallographic Details for Acids **2a–d**

	2a	**2b**	**2c**	**2d**
formula	$C_{10}H_6O_4$	$C_{11}H_{10}O_4$	$C_{12}H_{12}O_5$	$C_{10}H_8O_3$
mol wt	190	206	246	176
crystal system	triclinic	triclinic	monoclinic	triclinic
space group	$P\bar{1}$	$P\bar{1}$	$P2_1/n$	$P\bar{1}$
a	3.807 (2)	3.891 (1)	20.806 (6)	10.767 (3)
b	10.297 (2)	11.361 (3)	14.159 (3)	8.494 (3)
c	10.995 (3)	12.089 (4)	3.942 (5)	7.499 (2)
α	84.07 (2)	112.50 (2)	90	99.01 (2)
β	96.46 (3)	92.53 (3)	94.79 (7)	125.62 (2)
γ	98.13 (3)	96.12 (3)	90	112.42 (2)
cell volume, Å^3	422.3 (2)	488.8 (2)	1157.2 (4)	445.1 (2)
Z	2	2	4	2
$F(000)$	196	216	496	184
D_{calcd}, g cm^{-3}	1.49	1.40	1.41	1.31
λ, Å	0.7107	1.5418	0.7107	0.7107
μ, cm^{-1}	0.74	8.07	0.66	0.59
crystal size	0.52 × 0.25 × 0.22	0.88 × 0.28 × 0.10	0.63 × 0.26 × 0.12	0.68 × 0.57 × 0.19
diffractometer	CAD-4	CAD-4	P1	CAD-4
X-radiation	Mo Kα	Cu Kα	Mo Kα	Mo Kα
2θ range, deg	2–25	2–60	0–45	0–45
h	0–4	0–4	0–17	0–12
k	−12 to 12	−12 to 12	0–16	−9 to 9
l	−12 to 12	−13 to 13	−4 to 4	−8 to 8
total reflctn	1730	1770	1610	925
unique reflctn	1719	1707	1205	915
non-zero reflctn	746	1152	483	506
σ-level	3.0	2.0	3.5	2.0
R	0.056	0.040	0.066	0.058
R_w	0.057	0.044	0.067	0.053
min e Å^{-3}	−0.25	−0.24	−0.20	−0.44
max e Å^{-3}	0.12	0.25	0.19	0.31

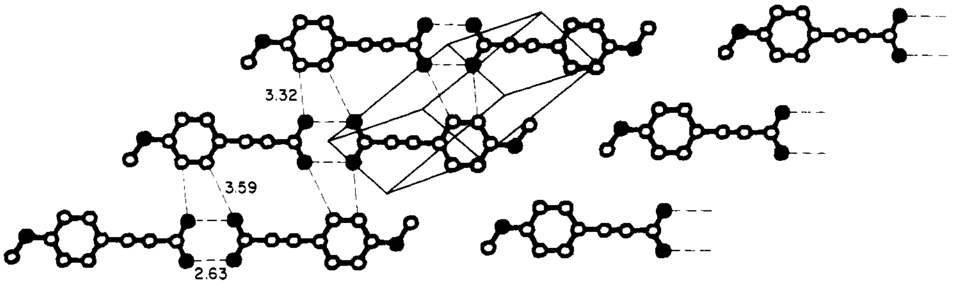

Figure 6. Layer structure of (4-methoxyphenyl)propiolic acid, **2d**. Unlike acids **2a–c**, the layers are inversion rather than translation stacked.

range 3.8–4.2 Å.[20] The difficulty in forming a stack here is because the internal methoxy group is constrained to lie out of the mean ring plane. Inspite of this constraint, acid **2c** adopts a translation-stacked layer structure because the large number of oxygen atoms are potential C–H···O bond acceptors. Figure 5 shows that the layer is stabilized by an extensive network of O–H···O (2.63 Å) and C–H···O (3.52, 3.89, and 3.92 Å) bonds. Interestingly, an out-of-plane methoxy hydrogen atom makes an additional shorter C–H···O contact of 3.42 Å with a methoxy oxygen atom of a stack-translated molecule. As in acids **2a** and **2b**, the carboxyl group is ordered (C–O 1.32 (2) and 1.23 (2) Å) and only the carbonyl oxygen has a C–H approach. The ordering of the carboxyl groups in acids **2a–c** is revealing and is indicative of the role of C–H···O interactions in discriminating between two alternative oxygen positions.[19]

Inspection of Figures 3–5 reveals the importance of C–H···O and also O–H···O hydrogen bonds in stabilizing layer structures for acids **2a–c**. The profusion of oxygen atoms contributes to the large number of such contacts. Almost all the hydrogen atoms are involved in these lateral interactions, which form an effective two-dimensional net, and these structures are notable for their lack of C···H interactions. The theme conveyed by these crystal structures is that *a critical number of oxygen atoms will permit a planar aromatic molecule to cross the structural threshold from a C···H-stabilized herringbone structure to a C–H···O-stabilized layer structure.*

The crystal structure of (4-methoxyphenyl)propiolic acid, **2d**, $C_{10}H_8O_3$, offers additional insight. The corresponding cinnamic acid, **1d**, $C_{10}H_{10}O_3$, forms a coronene-type structure in that the short axis is 4.8 Å.[17] This in itself is indicative of the importance of C···H interactions and suggests that the C:H:O ratio in **1d** is within the herringbone domain. The removal of two hydrogen atoms in acid **2d** does not appear to be sufficient to give a 4-Å structure. While molecular layers are formed from O–H···O hydrogen bonded molecules (O···O 2.63 Å; Figure 6), these layers are inversion stacked (as in acid **1b**, $C_{11}H_{12}O_4$[18a,c]) to give a short axis of 7.5 Å. These observations suggest that acids **2b** (translated stack), **1b**, **2d** (inverted stack), and **1d** (herringbone) lie in a structural series and that the inverted stack is structurally intermediate between the herringbone and translation-stack motifs. It is of interest to note that in contrast to acids **2a–c**, the carboxyl group in acid **2d** is disordered (C–O 1.27 (1) and 1.27 (2) Å). Figure 6 shows that the environment around each of the carboxyl group oxygens is nearly the same; C–H···O contacts from aromatic hydrogen atoms are possible at both oxygen positions (C···O 3.32 and 3.59 Å; H···O 2.81 and 2.64 Å). In this respect, the structure shows some similarity to that of 4-methylbenzoic acid.[21]

Almost predictably, the unsubstituted phenylpropiolic acid, **2e**, $C_9H_6O_2$, crystallizes with the herringbone pattern (short axis 5.113

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(20) Piplartine, CSD Refcode, CELVOE; Boll, P. M.; Hansen, J.; Simonsen, O.; Thorup, N. *Tetrahedron* **1984**, *40*, 171.

(21) Tavale, M. G.; Pant, L. M. *Acta Crystallogr., Sect. B* **1971**, *27*, 1152.

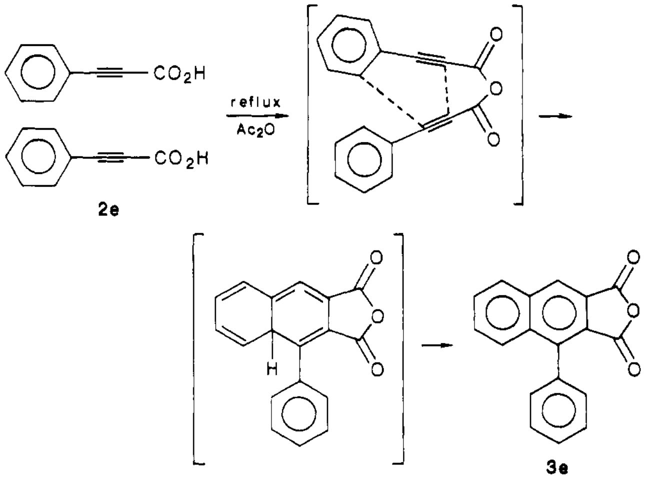
Table II. Solid-State Reactions of Acids **2a–e**[a]

acid	mp, °C[b]	short axis	structure solved[c]	reaction rate	T, °C[d]	distances, Å[e]	
						C7···C6	C7···C2
2a	165	3.807	yes	slow	>70	3.62	4.52
2b	155	3.891	yes	slow	>80	4.49	5.26
2c	141	3.942	yes	fast	>70	3.89	4.48
2d	139	7.499	yes	–	–		
2e	136	5.1	yes	–	–		

[a] See the text for reactions of related phenylpropiolic acids (4-methyl, 4-chloro, 2,4-dichloro, 3,4-dichloro). [b] These reported melting points are widely variable for acids **2a–c**. [c] Structures of acids **2a–d** were solved in this study. See ref 26 for structure of acid **2e**. [d] The reactions can be followed conveniently above this temperature, but proceed at lower temperatures also. [e] For designation of atom numbering, see Figure 7.

Å, *Pnnm*, $Z = 4$).[22] An early study by Rollett showed this molecule to be completely disordered at room temperature (ordered and $P2_1/n$ at −110 °C) and bisected by a crystallographic mirror plane. Pairs of molecules are centrosymmetrically hydrogen bonded and these dimers are the building blocks of the structure. However, the lack of a sufficient number of oxygen atoms results in a dovetailing of terminal phenyl groups so as to optimize C···H interactions. Accordingly, there is some similarity to the crystal structure of benzoic acid, a molecule not dissimilar in shape, size, and functionality (short axis 5.157 Å, $P2_1/c$, $Z = 4$).[23]

Solid-State Diels–Alder Reactions of Acids 1a–e. The motivation for engineering a 4-Å crystal structure for acids **1a–c** derived from the early observation of Haworth and Kelly that when phenylpropiolic acids (for instance **2e**) are refluxed with acetic anhydride, they are converted quantitatively to anhydrides (for instance **3e**) of the corresponding 1-phenylnaphthalene-2,3-dicarboxylic acids.[24] The chemical expedient of forming the symmetrical anhydride in situ brings diene and dienophile components together for a Diels–Alder reaction. By constructing a 4-Å short axis, it was hoped to achieve the same 4 + 2 cycloaddition in the crystalline acid itself. Extrapolating from the topochemical 2 + 2 cycloadditions of crystalline cinnamic acids, it was felt that intermolecular distances around 4.0 Å between diene and dienophile components would be within the critical reaction threshold, though one is dealing with photochemical and thermal processes in the two cases.[25]



2e **3e**

There is much evidence that crystalline phenylpropiolic acids decompose when heated. Variable melting points have been reported for at least 10 of them.[26] These variations appear to be heating rate dependent and are good pointers to solid-state reactivity. It was found that acids **2a–c** react when heated at temperatures as low as 80 °C to give anhydrides **3a–c** in 20–50% yields. In contrast, acid **1d** and the unsubstituted phenylpropiolic acid **1e** were found to be stable to heating in the solid state. Table II shows some typical reaction conditions for these solid-state Diels–Alder reactions. Acid **1a** is quite representative of the reactive compounds and may be considered further. Figure 7 shows the orientation of the incipient reactive centers. The triple bond in the reference molecule is the dienophile and the conjugated triple bond in the stack-translated neighbor is the diene. The arrangement is seen to parallel Haworth's original lignan synthesis very closely. We note that the distances from C7 of the reference molecule (x,y,z) to the two alternative reaction centers C6 and C2 of the stack neighbor ($1 + x,y,z$) are quite different, the values being 3.62 and 4.52 Å. Reaction at each of these centers would give isomeric anhydrides **3a** and **4a**. Of these, only **3a**, is observed and corresponds to reaction across the shorter distance of 3.62 Å. A similar situation is obtained for acid **2b**. The two relevant intermolecular distances C7···C6 and C7···C2 are 4.49 and 5.26 Å and only that product (**3b** rather than **4b**) is obtained, which corresponds to reaction across the shorter distance. In acid **2c**, reaction at either C2 or C6 gives the same product; the intermolecular C···C distances are 3.89 and 4.58 Å. It should be noted, however, that anhydrides **3a** and **3b** are also the sole products when acids **2a** and **2b** are refluxed with Ac$_2$O. To give anhydrides **3a–c**, the initial solid state 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.[27]

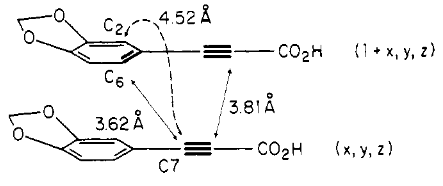
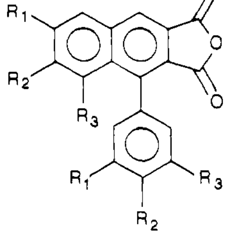


Figure 7. Schematic view of a topochemical Diels–Alder reaction for acid **2a**.



3a: $R_1, R_2 = -OCH_2O-$; $R_3 = H$
b: $R_1 = R_2 = CH_3O$; $R_3 = H$
c: $R_1 = R_2 = R_3 = CH_3O$
d: $R_1 = R_3 = H$; $R_2 = CH_3O$
e: $R_1 = R_2 = R_3 = H$
4a: $R_1 = H$; $R_2, R_3 = -OCH_2O-$
b: $R_1 = H$; $R_2 = R_3 = CH_3O$

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Table II shows that the three acids with 4-Å short axes react to give the corresponding Diels–Alder anhydrides while acids **2d** and **2e**, which do not have such short axes, are thermally stable. In the case of acid **2c**, the transformation is particularly rapid and no starting material is left after 5 days of heating at 90 °C. In all cases, the reaction proceeds noticeably at temperatures 50–100 °C below the "reported" melting point. It should be reemphasized that these reported melting points are purely artifacts and are governed by the heating rate. For instance, DSC shows that the reaction exotherm for acid **2a** (reported melting point 165 °C) occurs at 183, 174, or 152 °C, depending as to whether the heating rate is 20, 10, or 0.5 deg/min. Conversely, when a sample of acid **2a** is held at a constant lower temperature, reaction occurs over a period of time, an approximately 1:1 mixture of acid and Diels–Alder anhydride being produced in about 15 days at 120 °C or 30 days at 90 °C. Most interestingly, it was observed that a sample of acid **2a** which was allowed to remain under ambient laboratory conditions for 1 year (maximum summer temperature 43 °C) showed distinct signs of having reacted partially. The color of the sample changed from white to yellow-brown and changes in the X-ray powder pattern were obvious although owing to its complexity, the pattern could not be analyzed as a superposition of the spectra of acid **2a** and anhydride **3a**. However, HPLC traces showed the presence of the anhydride **3a** in this sample. We inferred that the reaction takes place in the solid state because the heated mixture remained free flowing below 120 °C and it was possible to record X-ray powder spectra at various stages of conversion.

An additional observation which attests to the solid-state nature of this thermal transformation is the stability to heat of the unsubstituted phenylpropiolic acid, **2e**. This acid has a short axis of 5.113 Å.[22] Neighboring molecules are presumably too far apart for a solid-state reaction and the acid may be maintained indefinitely below 120 °C without any change. Even above 120 °C, the only change observed was sublimation. The DSC shows only a sharp-melting endotherm at 136 °C in contrast to the reactive acids **2a–c**, all of which give reaction exotherms at varying temperatures. The DSC shows that there is absolutely no sign of the reaction occurring in liquid regions in a premelting stage. Yet, acid **2e** is converted to the Diels–Alder anhydride **3e** if refluxed with Ac_2O exactly like acids **2a–c**. So lack of reactivity of crystalline phenylpropiolic acid is not an intrinsic characteristic of the isolated molecule (lack of methoxy substituents, etc.) but seems to be governed by topochemical considerations. Similarly, acid **2d** is thermally stable, presumably because of a change in the crystal structure to an unreactive modification, but is converted by refluxing in Ac_2O to its corresponding Diels–Alder anhydride **3d**. We also noted that (4-methylphenyl)propiolic acid which does not adopt a 4-Å short axis (short axis 6.7 Å from Weissenberg photographs) is unreactive in the solid state. The melting point of this compound (150 °C) was unaffected by the heating rate and no change was observed on keeping at 90 °C for 4 weeks. On the other hand, (4-chlorophenyl)propiolic acid (short axis 3.944 Å, $R = 0.065$ on 831 non-zero reflections[28]) and (2,4- and (3,4-dichlorophenyl)propiolic acids (short axes 3.9 and 4.0 Å from Weissenberg photographs) were observed to react at 90 °C to yield the corresponding Diels–Alder anhydrides.

Considerable loss of material through sublimation and decarboxylation to the phenylacetylene occurs in these solid-state thermal processes. Decarboxylation of phenylpropiolic acids has been reported previously[29] and raises the question as to whether the 4 + 2 cycloaddition is topochemically controlled or occurs after a loosening of the structure following decarboxylation. Earlier work[30] on the thermal decomposition of unsubstituted acid **2e** in the melt shows that the yield of phenylacetylene is drastically reduced when the sample is heated in a stream of dry rather than moist N_2, perhaps suggesting that the Diels–Alder and decarboxylation reactions are unconnected processes which do not affect each other greatly. The present work strongly suggests a definite relationship between the crystal structures of acids **2a–e** and their behavior upon heating. However, it is difficult to establish mechanistic details of solid-state reactions based solely upon product distributions. It has been shown that the environment around reacting molecules may deviate from the ideal crystal structure even at very low conversions and that the course of a solid-state reaction could change dramatically even as it is proceeding.[31] Nevertheless, the unreactive behavior of acids **2d** and **2e** could be indicative of crystal-structure control at least in the initial stages of the reaction for acids **2a–c**.

Experimental Section

X-ray Crystallographic Studies on Acids 2a–d. Crystals suitable for X-ray work were obtained by recrystallization from EtOH in all cases. Data were collected for acids **2a** and **2b** at R.S.I.C., I.I.T. Madras on an Enraf Nonius CAD-4 diffractometer and for acids **2c** and **2d** at the Department of Chemistry, Ben Gurion University, on a Syntex P1 diffractometer. The structure solution of small planar molecules which form sheetlike layers continues to resist default settings in standard programs such as MULTAN80[32] and SHELXS86.[33] The three triclinic structures reported in this study proved problematic and were solved by reduction of the symmetry to $P1$, the position of the inversion centers being translated to an origin prior to refinement. Otherwise, the analyses were uncomplicated with hydrogen atoms being placed in calculated positions for acids **2c** and **2d**. All non-hydrogen atoms were refined anisotropically and the final R factors and other crystallographic information are presented in Table I. Tables of coordinates, bond lengths and angles, and F_o/F_c values for acids **2a–d** have been deposited as supplementary material.

Preparation and Solid-State Reactions of Acids 2a–e. These acids were prepared by literature procedures from the corresponding cinnamic acids by esterification with MeOH/HCl, bromination with Br_2/CH_2Cl_2, and dehydrobromination with NaH/EtOH under N_2. The solid-state reactions were carried out by taking approximately 100–500 mg of the powdered phenylpropiolic acids **2a–e** in round-bottomed flasks. The flasks were lightly plugged with cotton and kept in oil baths at appropriate temperatures between 70–110 °C. Within 2–7 days, the samples became discolored and some sublimed acid and phenylacetylene could be seen coated at the top of the flask. The mixtures were stirred occasionally, and after 4–6 weeks, the reaction mixtures were separated by column chromatography. The following reaction details were noted for acids **2a–c** (acid, percent conversion to Diels–Alder anhydride, percent unreacted plus sublimed acid, time of reaction, temperature of reaction): **2a**, 25%, 32%, 5 weeks, 95 °C; **2b**, 30%, 25%, 6 weeks, 90 °C; **2c**, 20%, 30%, 3 weeks, 90 °C. Authentic samples of the Diels–Alder anhydrides **3a–e** were prepared by refluxing acids **2a–e** with Ac_2O for 3–6 h according to literature procedures.[24] All compounds were characterized by NMR and mass spectroscopy and by comparison with authentic samples. Other details of these experiments are summarized in Table II.

Conclusions

C–H···O interactions may be utilized to design layered crystal structures for a series of (alkoxyphenyl)propiolic acids. These structures are characterized by a short axis of ca. 4 Å. A chemical consequence of this structure is that triple bonds in stack-translated molecules can participate in an intermolecular Diels–Alder reaction. This behavior is representative of a new class of solid-state transformations which may not only be deliberately engineered but may also be of considerable interest in lignan biosynthesis.

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Supplementary Material Available: Full tables of crystallographic data for acids **2a–d** including atomic coordinates, bond lengths and angles, and anisotropic thermal parameters (17 pages); listing of F_o/F_c values (15 pages). Ordering information is given on any current masthead page.

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