$$\frac{a_3}{a_2} = \left\{k_A \frac{(k_2 - \lambda_a)}{k_{EA}[B]} + k_E\right\} \frac{1}{k_F - \lambda_a}$$

With eq 8, this becomes

$$\frac{a_2}{a_3} = \frac{k_{EA}[B](k_F - \lambda_a)}{k_A(k_2 - \lambda_a + Z)} \tag{A38}$$

The boundary condition (eq A34) gives

$$\frac{b_2}{a_2} = -1 \tag{A39}$$

From eq A24b, one gets

$$\frac{b_1}{b_2} = \frac{k_2 - \lambda_b}{k_{EA}[B]} \tag{A40}$$

Dividing eq A24c by b_2, and replacing b_1/b_2 by its value above, one has

$$\frac{b_3}{b_2} = \left\{k_A \frac{(k_2 - \lambda_b)}{k_{EA}[B]} + k_E\right\} \frac{1}{k_F - \lambda_b}$$

or

$$\frac{b_3}{b_2} = \frac{k_A(k_2 - \lambda_b + Z)}{k_{EA}[B](k_F - \lambda_b)} \tag{A41}$$

Using eq A38, A39, and A41, eq A36 can now be rewritten

$$\frac{b_3}{a_3} = -\frac{(k_F - \lambda_a)(k_2 - \lambda_b + Z)}{(k_F - \lambda_b)(k_2 - \lambda_a + Z)} \tag{A42}$$

In these experiments with cyclohexanone and mesitylene, $k_F >> \lambda_{a,b}$. Thus, eq A42 can be further simplified to

$$Z = \frac{(k_2 - \lambda_a) + \beta(k_2 - \lambda_b)}{1 + \beta} \tag{9}$$

From the boundary conditions, eq A33 and A34, one calculates R, as defined by eq 11:

$$R = \frac{a_3 + b_3 + c_3}{a_1 + b_1}$$

which rearranges to

$$R\left(\frac{a_1}{a_3} + \frac{b_1}{a_3}\right) = 1 + \frac{1}{\beta} + \frac{c_3}{a_3} \tag{A43}$$

Since $b_2/a_2 = -1$ (eq A39)

$$\frac{a_1}{a_3} + \frac{b_1}{a_3} = \frac{a_1 a_2}{a_2 a_3} - \frac{b_1 b_2 a_2}{b_2 a_2 a_3} = \frac{a_2}{a_3}\left(\frac{a_1}{a_2} - \frac{b_1}{b_2}\right) \tag{A44}$$

Using eq A37, A38, and A40, this equation becomes

$$\frac{a_1}{a_3} + \frac{b_1}{a_3} = \frac{(k_F - \lambda_a)(\lambda_b - \lambda_a)}{k_A(k_2 - \lambda_a + Z)} \tag{A45}$$

The ratio c_3/a_3 in eq A43 can be written

$$\frac{c_3}{a_3} = \frac{c_3 b_3}{b_3 a_3}$$

or, from the definitions of α and β (eq A29 and A30)

$$\frac{c_3}{a_3} = \frac{\alpha}{\beta} \tag{A46}$$

With eq A45 and A46, eq A43 becomes

$$\frac{R(k_F - \lambda_a)(\lambda_b - \lambda_a)}{k_A(k_2 - \lambda_a + Z)} = 1 + \frac{1 + \alpha}{\beta}$$

In these experiments $k_F >> \lambda_a$ and $\alpha >> 1$; therefore

$$\frac{k_F R(\lambda_b - \lambda_a)}{k_A(k_2 - \lambda_a + Z)} = \frac{\alpha}{\beta}$$

or

$$k_A = \frac{\beta k_F R(\lambda_b - \lambda_a)}{\alpha(k_2 - \lambda_a + Z)} \tag{10}$$

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Registry No. Cyclohexanone, 108-94-1; mesitylene, 108-67-8; 9,10-dibromoanthracene, 523-27-3; cyclohexanone·mesitylene complex, 89891-17-8.

The Use of Mixed Crystals for Engineering Organic Solid-State Reactions: Application to Benzylbenzylidenecyclopentanones

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Abstract: The concept of chloro/methyl group interchange as a tool in crystal engineering is discussed with respect to derivatives of 2-benzyl-5-benzylidenecyclopentanone (**1**–**4**). A study of the mixed crystals containing either **1** and **2** (X) or **3** and **4** (Y) demonstrates that molecules which otherwise crystallize into photostable crystal structures may be incorporated into a light-sensitive form. Furthermore, such mixed crystals are demonstrated (using four-circle diffractometry) to undergo single-crystal → single-crystal reaction with the formation of the product dimer molecules identified within the reactant lattice. The final R for X is 0.0418, for Y it is 0.0578, and for irradiated X it is 0.0394.

It is clear that the controlled variation of the substituent groups present on an organic molecule may allow subsequent crystallization into particular and desired packing arrangements[2]. One particular strategy for this so-called crystal-engineering concept

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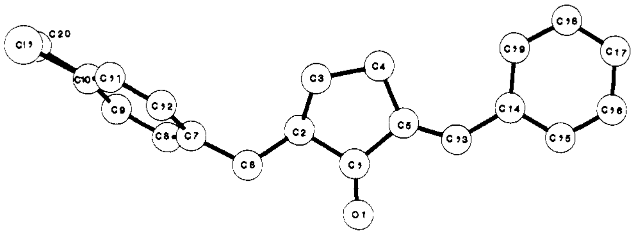


Figure 1. Atom numbering scheme for X and Y.

is the interchange of such groups as chloro and methyl,[3,4] both substituents having relatively similar van der Waals radii. In certain cases, however, such volume considerations per se are not adequate, and other factors—notably electronic—must be considered. Such a close interplay of both spatial and electronic factors[5] has recently been clearly demonstrated in a family of compounds based upon 2-benzyl-5-benzylidenecyclopentanone (BBCP)[6].

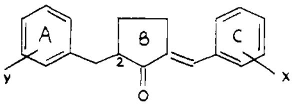
In addition, a study of several derivatives of BBCP has enabled, for the first time, a detailed systematic study to be made of the crystallographic course of a [2 + 2] photocycloaddition reaction, such that the gradual formation (to 100% conversion) of the photoproduct may be monitored. The general conclusions resulting from this work have been described elsewhere.[7]

In this paper we extend this type of study to crystals composed of solid solutions of various benzylidenecyclopentanones which differ only in so far as chloro or methyl interchange. What emerges is a new strategy for incorporating molecules into particular packing motifs which would otherwise be unobtainable and clear evidence for complete conversion (in a single-crystal → single-crystal fashion) of the mixed reactant material.

Experimental Section

The cyclopentanones **1** to **4** were prepared as previously described[3a] and were recrystallised from 1:1 $CHCl_3$/MeOH. Mixed crystals of the pairs **1**, **2** and **3**, **4** were grown from the slow evaporation of a dilute solution in the same solvent. Melting points of solids obtained from varying amounts of **1** and **2** were determined by DSC on a Perkin-Elmer DSC1B instrument. The melting points were calibrated by using a standard benzoic acid sample.

		X	Y
1	pMeBBCP	H	pMe
2	pClBBCP	H	pCl
3	pMeBpBrBCP	pBr	pMe
4	pClBpBrBCP	pBr	pCl



Crystallographic Details: Preliminary unit cell and space group data were obtained from oscillation and Weissenberg photographs. Accurate cell parameters and intensity data were obtained on an Enraf-Nonius CAD-4 diffractometer in the manner described elsewhere.[8] No absorption correction was carried out. Some refinement details are closely connected with the structure of the mixed crystals, and these are therefore given later in the text. All non-hydrogen atoms were assigned anisotropic thermal parameters (except for those with occupancy 0.2 in X after irradiation), whereas hydrogen atoms, which were located from difference Fourier maps, were refined isotropically. For crystal Y, it was found necessary to constrain the hydrogen atoms to ideal bond lengths and angles. For X after irradiation, the hydrogen atoms were fixed during the final least-squares cycle. The refinement method used throughout was full-matrix least squares. Occupancy factors, where relevant, were allowed to refine during least-squares cycles until they converged and were thereafter fixed. All calculations were performed on an IBM 3081 computer (University of Cambridge) with use of SHELX-76 (G. M. Sheldrick), PLUTO-78 (W. D. S. Motherwell), and private programs. Scattering factors were obtained from the "International Tables for X-ray Crystallography".[13] Crystal and refinement details are given in Table I, and the atom numbering scheme is shown in Figure 1. Most crystals of the BBCP series are platelets, and as a result, the crystals used in this work all had thickness of only 0.05 mm. A weighting scheme was used for Y but not for X, because variance statistics indicated that this was necessary for Y but not for X.

Table I. Crystal and Refinement Data

	X	Y	X irradiated
components	**1**, **2**	**3**, **4**	**1**, **2**, dimer
space group	$P2_1/c$	$P2_1/c$	$P2_1/c$
a, Å	17.314 (2)	18.365 (7)	17.306 (3)
b, Å	10.667 (1)	11.152 (2)	10.667 (2)
c, Å	8.747 (2)	8.324 (2)	8.768 (2)
β, deg	77.39 (2)	94.51 (3)	76.64 (2)
V, Å^3	1576.5	1699.5	1574.8
Z	4	4	4
$F(000)$	608	744	608
μ, cm^{-1}	12.30	37.64	12.31
data unique	2186	2345	2075
data obsd	1103	1185	1107
significance test	$F_o > 1.5\sigma(F_o)$	$F_o > 2\sigma(F_o)$	$F_o > \sigma(F_o)$
no. of parameters	267	206	219
crystal size, mm	0.30 × 0.20 × 0.05	0.25 × 0.25 × 0.05	
wt scheme	unit weights	$[\sigma F^2 + 0.0005F^2]^{-1}$	unit weights
occupancies			
Cl	0.36 (3)	0.30 (3)	0.36
methyl	0.64 (3)	0.70 (4)	0.64
monomer	1.00	1.00	0.80 (4)
dimer	0.00	0.00	0.20 (4)
R	0.0418	0.0575	0.0394
R_w		0.0518	

Crystals X and Y were irradiated in situ on the four-circle diffractometer with light from a 100W low-pressure mercury lamp filtered through Pyrex. The crystals were continuously rotated during irradiation to ensure uniform exposure to light. Accurate cell parameters were periodically determined, and irradiation was arrested when a significant change in cell parameters was achieved; full intensity data were then collected. In the case of UV-irradiated Y the crystal faded exponentially with the result that it was impossible to obtain a full set of intensity data.

Discussion

1. Solid Solution Formation and the Interchangeability of Chloro and Methyl Groups. Compounds **1** and **2** differing only in the identity of the substituent Y (Cl or CH_3) attached to C(10) crystallize in isomorphous structures. Both compounds are photoreactive in the solid state, with potentially reactive double bonds related by a center of symmetry and within 4.1 Å of one another.[6,9] For both compounds, centrosymmetric cyclobutane dimers are formed in a homogeneous single-crystal to single-crystal transformation. This type of behavior is a characteristic of the BBCP family of structures and has been described previously.[7,9b]

When **1** and **2** are taken in varying amounts in solution and allowed to slowly evaporate to dryness, the melting points of the solid residues obtained vary smoothly and linearly between those of pure **1** (113 °C) and pure **2** (127 °C), indicating ideal solid solution behavior.

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Table II. Crystal Data for **1–4**

	space group	*a*, Å	*b*, Å	*c*, Å	*β*, deg	*V*, Å^3
1	$P2_1/c$	17.341 (2)	10.675 (1)	8.736 (1)	102.54 (1)	1578.6
2	$P2_1/c$	17.175 (4)	10.587 (3)	8.796 (5)	76.33 (9)	1554.1
3	$P2_1/c$	18.381 (2)	11.209 (2)	8.285 (2)	94.46 (1)	1701.9
4	$P2_1/c$	17.522 (4)	7.906 (2)	11.888 (2)	91.19 (1)	1646.4

"Mixed" crystals suitable for X-ray studies may also be grown from solutions containing **1** and **2**, and such a crystal X obtained from a solution containing equimolar amounts was examined by X-ray methods. The cell dimensions for X are intermediate between those for pure **1** and **2** (Table II), and Weissenberg photographs for this crystal were characteristically different from those for either **1** or **2**. This was confirmed upon full data collection.

The atomic coordinates (excluding the methyl carbon C(20)) previously obtained for the crystal structure[9b] of pure **1** were used as the starting model. When a difference map was computed for X by using these coordinates, two peaks at approximately 1.5 and 1.7 Å from C(10) and separated from each other by 0.60 Å were clearly revealed. These were assigned to the methyl carbon and the chlorine. The refinement of the occupancy factors proceeded satisfactorily, with that of Cl given the value x and that of C(20) the value of $(1 - x)$, and showed that X contains approximately 66% **1** and 34% **2**. The positions of all other atoms were not significantly different from those obtained for pure **1** or **2**. Refinement converged at $R = 0.0418$, while refinement of the intensity data for X assuming a single phase composition and using the coordinates of only **1** or **2** was not satisfactory (since convergence was achieved at a significantly higher R) and confirms that we are dealing with a truly mixed crystal.

It is possible, therefore, to continuously substitute **1** for **2**, and vice versa, in the solid state and form true solid solutions for all compositions. The methyl–chloro interchange is, therefore, valid in this case with the individual structures being isomorphous and the mixed crystals consituting a structural continuum between the pure compounds. The nature of the incipient dimer present within the mixed crystal is, therefore, unchanged from that present in the pure crystals . [The mean separation of the (centrosymmetrically related) reactive centers is 4.071 Å.]

2. Crystal Engineering. The behavior of the pair of compounds **3** and **4**, however, is more subtle, since the crystal structures of pure **3** and pure **4** are quite different.[10] Ketone **3** crystallizes in a photoactive modification, with a unit cell, molecular conformation (Figure 2a) and reactive center separation that are very nearly the same as for **1** and **2** described above (the slight difference in the *a* axis resulting from the additional bromine atom in **3**). Compound **4**, however, crystallizes in a photostable form[10] and in a conformation (Figure 2b) that is quite different from that of **1**, **2**, or **3**.[3a,9] (This conformation has been shown[6] to result from certain non-bonded atom–atom interactions which occur in the crystal structure of 4 but not of **3**.) Consequently methyl–chloro interchange is not valid for **3** and **4** because both electronic and volume factors seem to be important.[6,9b,10]

It is therefore quite significant that when solutions containing 90% of **3** and 10% of **4** are carefully evaporated, mixed crystals which incorporate both compounds are obtained. Compound **4** is appreciably less soluble in the solvent of choice (1:1 $CHCl_3$–MeOH), this dictating the relative amounts of **3** and **4** used. In about 24 h, well-formed crystals which morphologically resemble crystals of pure **3**, were obtained.

When a crystal Y from this batch was examined it was found that the cell dimensions were significantly different from those of pure **3** or pure **4**, and the collection of intensity data additionally indicated significant differences for the corresponding structure factor amplitudes between crystals Y and **3**. The structure of Y was subsequently solved by Patterson methods; no starting model was used. The atoms in the BBCP skeleton were found in positions resonably similar to the structure of **3**. When these were introduced into difference Fourier syntheses, peaks corresponding to statistically averaged chlorine and methyl carbons were obtained. The occupancy factors were refined as previously described. The bond lengths C(10)–Cl(1) and C(10)–C(20) were reasonable chemically (1.70 and 1.50 Å, respectively) and confirm a solid solution structure for Y (Figure 2c). The final refinements converged at $R = 0.0575$ ($R_w = 0.0518$). Final occupancies for C(20) and Cl(1) were 0.70 and 0.30, respectively. It therefore is clear that the packing in Y is essentially similar to that of **3**, with the reactive centers in the mixed structure separated by 3.866 Å.

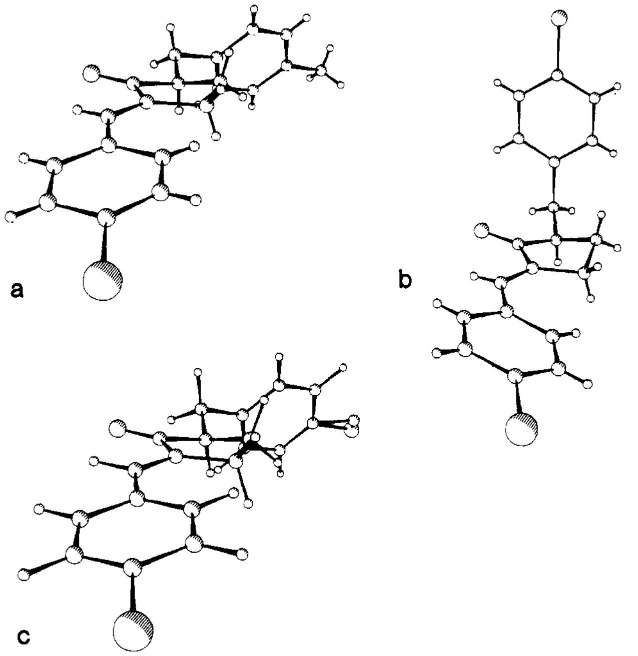

Figure 2. Molecular conformations in the crystal structures of (a) pure **3**, (b) pure **4**, and (c) mixed crystal Y to show how the conformation of **4** has been altered by going to the mixed crystal. the dihedral angles subtended by the benzylidene moiety and the benzyl phenyl rings are 70° for **3**, 98° for **4**, and 72° for Y.

We note that as a consequence of co-crystallization, the chloro compound **4** has been induced to adopt both the crystal structure and molecular conformation of the methyl derivative **3**. Although the amount of **4** present in solution was only 10%, it was incorporated into Y to an extent of 30%. Clearly, the methyl derivative **3** plays a critical role in steering the structure of the mixed crystal Y toward that of its own structure, while simultaneously incorporating increasing amounts of a molecule that would prefer to adopt a different structure if taken separately. Chloro–methyl interchange is, therefore, possible despite the energy which is lost as a result of the absence of some favorable non-bonded interactions.

Although it is speculative to comment in detail, it is worthwhile to consider the crystallization process that led to the formation of mixed crystal Y. Ketone **4** can adopt both a "linear" and a "bent" conformation, the latter being adopted in its native photostable crystal structure. **3** adopts a "linear" conformation which results in a photoactive structure (Figure 2). Since the "bent" and "linear" forms of **4** do not differ greatly in energy, the compound may have a **3** polymorph, not normally obtained on crystallization, but which is here seeded by **3**. Thus, co-crystallization may take place.

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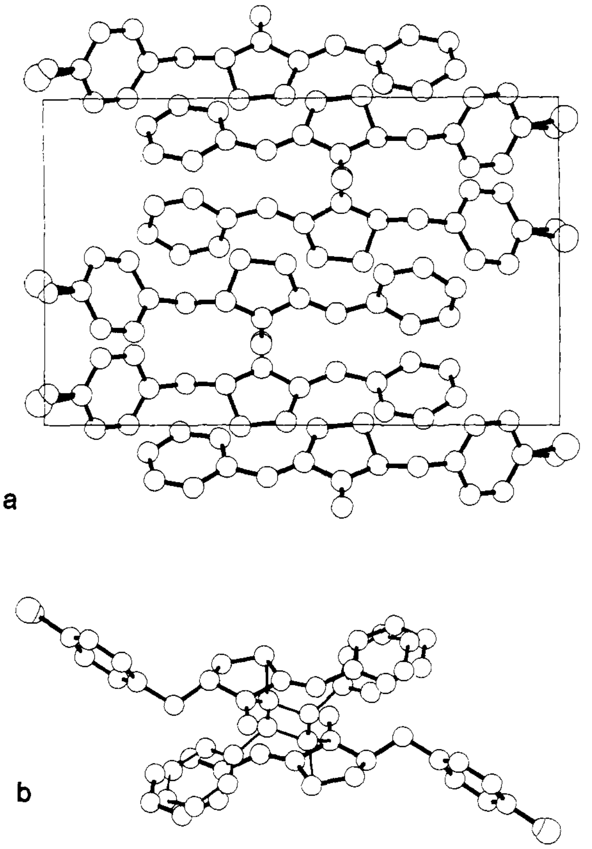

Figure 3. (a) Crystal structure of X viewed along *c* and (b) the dimer and incipient dimer for X after irradiation, as obtained by X-ray studies.

The incorporation of 30% of **4** in Y occurs even though it is present in only 10% quantity in solution. There may be mixed crysals that contain differing amounts of **3** and **4**. Y was chosen from the first crop and it is expected that many crystals in this batch would contain amounts of **4** greater than 10%, since **4** is much less soluble than **3**. Owing to practical difficulties it was not possible to examine several crystals by single crystal diffractometry to determine the relative amounts of **3** and **4**. However, Weissenberg photographs of a few crystals, randomly selected from this first crop, were very similar.

3. Dynamic Studies. The structures of the partially reacted crystals X and Y were solved by using as a starting model the monomer carbon framework, including the substituents, but excluding atoms C(5) and C(13). For X, atoms C(5) and C(13) were located after one cycle of least-squares refinement at positions similar to those found for the nonirradiated crystal. Their positional and thermal parameters as well as occupancies were refined. As a result two new peaks subsequently appeared close to C(5) and C(13) corresponding to the same atoms (designated as C(5′) and C(13′)) now as part of the product dimeric molecule. The occupancy factor of these two atoms was set at $(1 - x)$, x being the occupancy factors for the two atoms in the monomer framework. Positional and thermal parameters as well as occupancy factors for C(5′) and C(13′) were next allowed to vary. At this stage, peaks appeared near atoms C(14) to C(19) (designated as C(14′) to C(19′)) corresponding to the positions for these atoms in the dimer molecule. Ring C(14′)···C(19′) was treated as a rigid body during refinement. Therefore, atoms C(14) to C(19) were refined at two alternative positions, one corresponding to the monomer, with occupancy x, and one corresponding to the dimer, with occupancy $(1 - x)$. x was finally refined to 0.8. For the benzyl group, the thermal parameters are consistently higher in the crystal after reaction than before, possibly indicating the presence of a second phenyl ring too close to the first for resolution. For crystal Y, it was impossible to locate the dimer positions for C(5) and C(13) due to incomplete data, but the occupancy factor of C(5) and C(13) refined to a value significantly less than 1. The crystal structure of X before irradiation is shown in Figure 3a. Figure 3b shows the dimer and incipient dimer in X after irradiation.

In order to establish that reaction has indeed occured in X upon photoirradiation, as well as to confirm the homogeneity of the solid solution, single crystals from the same batch as that from which the single crystal of X was obtained were irradiated under comparable experimental conditions to those used above and then studied by mass spectroscopy.

Strong peaks were observed at *m/e* 276 (assigned to pMeBBCP) and *m/e* 296 (assigned to pClBBCP) of roughly equal intensity. In addition, strong peaks were observed at *m/e* 592 (pClBBCP dimer, highest *m/e* present) and *m/e* 552 (pMeBBCP dimer) and also at *m/e* 572 which may be assigned to the mixed dimer of pClBBCP and pMeBBCP. The peak at *m/e* 572 had satellites at M + 1, M + 2, and M + 3 in the intensity pattern expected for chlorinated species. This indicates that dimerization has indeed occurred in the solid state. Furthermore, the peak at *m/e* 572 is stronger than either of the other two dimeric peaks, suggesting, as expected, that mixing of pClBBCP and pMeBBCP in these crystals is random. Each of the irradiated single crystals will have a slightly different concentration of chloro and methyl compounds (e.g., X has 36% Cl and 64% Me, while other crystals we have studied had pClBBCP content varying from 12% to 64%). This will account for the presence in the mass spectrum of dimeric peaks which correspond to the two pure dimers.

Concluding Remarks

These results show that the strategy of mixed-crystal formation may be successfully used to incorporate molecules into new and photoactive modifications. They further show that partially reacted mixed crystals may be fairly accurately represented by a model in which monomer and dimer molecules exist in a statistically disordered fashion. They also indicate that the photodimerization of these BBCP derivatives proceeds in a single-crystal to single-crystal fashion, in accordance with previous measurements,[11] in a homogeneous fashion. Curiously, when partially reacted crystals of the parent nonsubstituted benzylidene compounds are analyzed in a similar fashion, it was not possible to satisfactorily model their structure, using least-squares refinement techniques.[7] The distinction between these two cases is not entirely clear, and could lie in factors as subtle as reaction rates and exact irradiation conditions or the differences in geometry of the incipient dimers. It may, furthermore, highlight the potential use of such mixed crystals in overcoming some of the difficulties associated with lattice mismatch between reactant and product.[12] Finally, we note, using these mixed crystals, the formation, in high yield, of pseudo-inversion-symmetry cyclobutanes as products of the reaction.

Acknowledgment. We thank Professor J. M. Thomas for many useful discussions and acknowledge the financial support of the SERC and the University of Cambridge. The financial support of the British Council (to G.R.D.) is appreciated.

Registry No. 1, 78943-54-1; **2**, 78943-55-2; **3**, 78943-52-9; **4**, 78943-53-0.

Supplementary Material Available: Tables of final atomic parameters and lists of bond lengths, bond angles, and observed and calculated structure factors (33 pages). Ordering information is given on any current masthead page.

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