Tetrahedron Vol. 49, No. 5, pp. 987-994, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

DIELS-ALDER CYCLOADDITIONS OF CYCLOPENTADIENES TO DMAD TETRAMER

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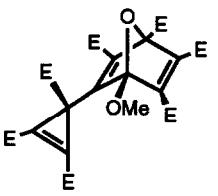
(*Received in USA* 21 *October* 1992)

Abstract: Thermal reactions of 5-(trimethylsilyl)cyclopentadiene and of cyclopentadiene with DMAD tetramer (**1**) each result in Diels-Alder cycloaddition folowed by intramolecular hetero Diels-Alder reaction in which a "1-oxabutadiene" moiety cycloadds to the endo face of the norbornene C=C double bond, thereby affording **3** and **4**, respectively. Selective hydrolysis of the ketene acetal and/or ketal functionalities in **3** and **4** has been performed. The structures of **3** and of two hydrolysis products, **5** and **6**, have been established via X-ray crystallographic methods.

Introduction. The fact that dimethyl acetylenedicarboxylate (DMAD) undergoes spontaneous tetramerization has been known for many years.[1] In 1968, this tetramer was shown by Kauer and Simmons[2] to possess structure **1**. Despite its interesting and complex structure, the organic chemistry of tetramer **1** has received surprisingly little attention since that time. We now report the results of our studies of Diels-Alder cycloadditions of 5-(trimethylsilyl)-cyclopentadiene and of cyclopentadiene to **1**.



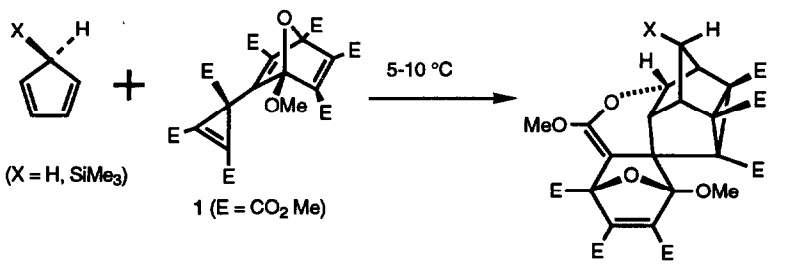
1 (E = CO_2 Me)

Results. Our interest in DMAD tetramer was sparked by observations made during the course of a synthesis of dimethyl *anti*-7-(trimethylsilyl)-norbornadiene-2,3-dicarboxylate (**2**).[3] When 5-(trimethylsilyl)cyclopentadiene was reacted with monomeric DMAD in benzene at 0-10 °C, we noted that a small amount of a colorless solid, **3** (mp 211-212 °C), was obtained along with the expected Diels-Alder cycloadduct , **2**. The proton NMR spectrum of this solid was surprisingly complex. A total of *eight* singlets were observed in the region δ 3.5-3.9, which corresponds to the presence of eight magnetically nonequivalent -OMe groups in **3**. The proton noise-decoupled ^{13}C NMR spectrum of **3** is also complex and contains a total of 30 individual resonances (see the Experimental Section).

Subsequently, we found that **3** could be synthesized directly via Diels-Alder cycloaddition of 5-(trimethylsilyl)cyclopentadiene to authentic DMAD tetramer (which was synthesized by using the procedure described by Kauer and Simmons).[2] The structure of **3** was established unequivocally via single crystal X-ray structural analysis.

We have also studied the corresponding Diels-Alder cycloaddition of the parent (unsubstituted) cyclopentadiene to tetramer **1**. This reaction afforded a single product whose ^1H and ^{13}C NMR spectra closely parallel the corresponding spectra of **3**. On this basis, we assign structure **4** (Scheme 1) to this compound.

Scheme 1



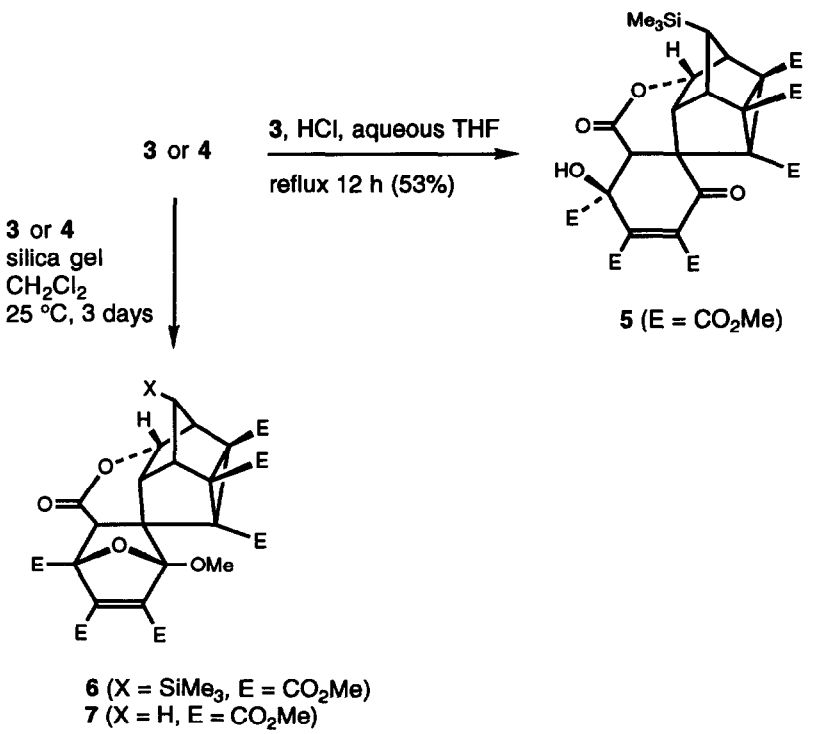
3 (X = $SiMe_3$, E = CO_2Me; 47%)
4 (X = H, E = CO_2Me; 67%)

Acid Hydrolysis of 3 and 4. Acidic hydrolysis was performed by refluxing **3** with dilute aqueous HCl for 12 h. This procedure afforded **5** (Scheme 2), which resulted simply via hydrolysis of both the ketene acetal and the ketal functionalities in **3**. The structure of **5** was established unequivocally via single crystal X-ray structural analysis.

When acidic hydrolysis of **3** was performed under less stringent conditions (i.e., wet silica gel[4]), selective hydrolysis of the ketene acetal moiety occurred, leaving the ketal group intact (see the Experimental section). The structure of the product, **6**, thereby obtained was established via X-ray crystallographic methods. Mild acidic hydrolysis of **4** similarly resulted in selective hydrolysis of the ketene acetal moiety, thereby affording **7** (Scheme 2).

In each of the X-ray structures of **3**, **5** and **6**, the norbornane ring is highly distorted due to the presence of the fused five-membered ring. The relative bond length variations in the best refined structure, **6**, are reproduced by molecular mechanics calculations (MM3).[5]

Scheme 2

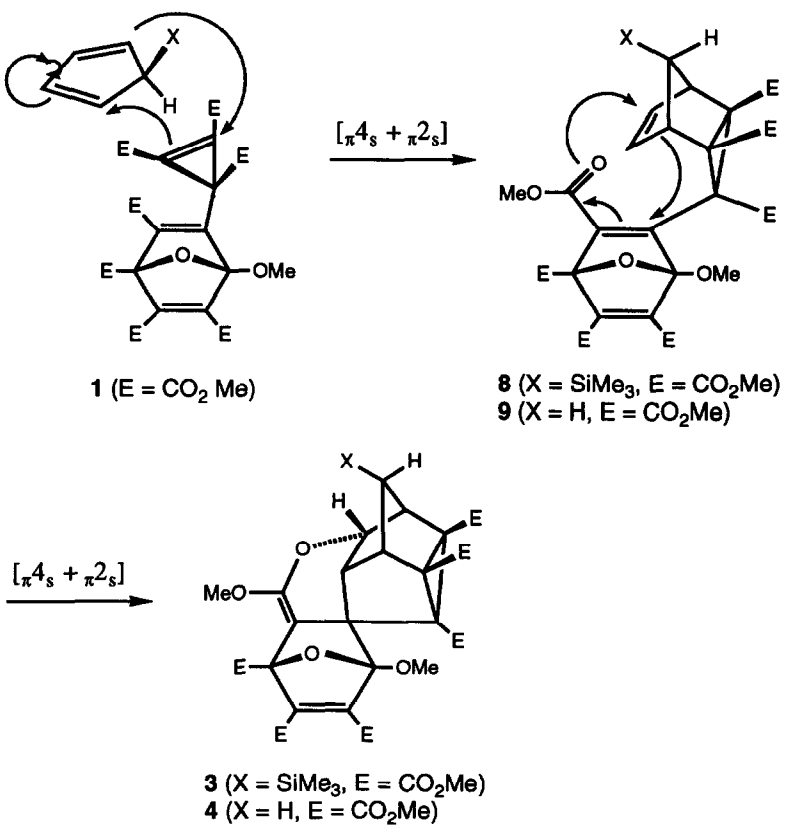


5 (E = CO_2Me)

6 (X = $SiMe_3$, E = CO_2Me)
7 (X = H, E = CO_2Me)

Discussion. A mechanism is shown in Scheme 3 which accounts for the formation of **3** and of **4** via reactions of **1** with 5-(trimethylsilyl)cyclopentadiene and with cyclopentadiene, respectively. In each case, initial Diels-Alder cycloaddition occurs in accordance with the Alder-Stein principle of "maximum accumulation of unsaturation"[6] to afford the corresponding endo [4 + 2] cycloadduct (i.e., **8** and **9**, respectively). Neither **8** nor **9** is isolated; instead, each intermediate undergoes further intramolecular hetero Diels-Alder reaction in which a "1-oxabutadiene" moiety ("heterodiene")[7] cycloadds to the endo face of the norbornene C=C double bond (dienophile). Such reactions are well precedented; there are several reported examples in which α,β-unsaturated carbonyl compounds, functioning as "1-oxa-butadienes",[7] undergo inter- or intramolecular [4 + 2] cycloadditions to isolated alkene C=C double bonds (which function as the dienophile).[8]

Scheme 3



1 (E = CO_2 Me)

8 (X = $SiMe_3$, E = CO_2Me)
9 (X = H, E = CO_2Me)

3 (X = $SiMe_3$, E = CO_2Me)
4 (X = H, E = CO_2Me)

It is known that the presence of a 7-(trimethylsilyl) substituent in an appropriately functionalized norbornene can effectively promote retro-Diels-Alder reaction by exerting a "β-effect". Thus, the electronic effect of the $SiMe_3$ group lowers the activation energy for such retro-Diels-Alder reactions by selective stabilization of positive charge which develops on a carbon atom situated β to the $SiMe_3$ group.[9] As noted above, we observe that cyclopentadiene cycloadds to **1** under mild conditions to afford a product, **4**, which is analogous to that which is formed under comparable conditions when 5-(trimethylsilyl)cyclopentadiene is reacted with **1**. Thus, it is not necessary to invoke any special stabilizing electronic effect by the $SiMe_3$ group in order to account either for the initial Diels-Alder reaction of the subsequent hetero-Diels-Alder reaction which leads to the formation of **3** via reaction of 5-(trimethylsilyl)cyclopentadiene with **1**.

Experimental Section

Melting points are uncorrected.

Diels-Alder Cycloaddition of 5-(Trimethylsilyl)cyclopentadiene to DMAD Tetramer (1). A solution of 5-(trimethylsilyl)cyclopentadiene[10] (1.0 g, 5.7 mmol) in dry benzene 2 mL) was cooled externally to 10 °C. To this cooled solution **1** (150 mg, 0.26 mmol) was added with stirring, and the resulting mixture was stirred at 10 °C for 1 h. The reaction mixture then was placed in a refrigerator for 24 h. Hexane (25 mL) was added, whereupon a colorless solid precipitated. The precipitate was collected via suction filtration and then recrystallized from CH_2Cl_2-hexane. Pure **3** (85 mg, 47%) was thereby obtained as a colorless microcrystalline solid: mp 211-212 °C; IR (KBr) 1737 (sh, vs), 1716 (vs), 1450 (m), 1330 (s), 1268 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 0.05 (s, 9 H), 1.62 (d, J = 3.0 Hz, 1 H), 2.28 (dd, J_1 = 6.0 Hz, J_2 = 2.5 Hz, 1 H), 3.19 (m, 1 H), 3.38 (m 1 H), 3.50 (s, 3 H), 3.54 (s, 3 H), 3.58 (s, 3 H), 3.61 (s, 3 H), 3.68 (s, 3 H), 3.72 (s, 3 H), 3,79 (s, 3 H), 3.84 (s, 3 H), 4.33 (dd, J_1= 4.5 Hz, J_2= 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ -1.23 (q), -1.23 (d), 43.14 (d), 46.37 (d), 48.10 (s), 50.14 (d), 51.24 (q), 51.96 (q), 52.28 (q), 53.27 (q), 52.86 (q), 53.03 (q), 54.34 (s), 55.46 (q), 56.27 (q), 57.77 (s), 60.13 (s), 81.94 (d), 82.63 (s), 89.24 (s), 114.02 (s), 133.27 (s), 153.39 (s), 154.70 (s), 160.39 (s), 163.86 (s), 165.47 (s), 165.83 (s), 167.92 (s), 168.17 (s). Anal. Calcd for $C_{32}H_{38}O_{16}Si$: C, 54.38; H, 5.42. Found: C, 54.17; H, 5.31.

Acidic Hydrolysis of 3. Method A. To a solution of **3** (200 mg, 0.28 mmol) in THF (7 mL) was added 5% aqueous HCl (0.5 mL, excess), and the resulting mixture was refluxed for 12 h. The reaction mixture was allowed to cool to room temperature and then was concentrated in vacuo. Water (3 mL) was added to the residue, and the resulting mixture was extracted with CH_2Cl_2 (3 x 3

mL). The combined organic extracts were washed with water (3 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel by eluting with 2:3 EtOAc-hexane. Unreacted **3** (70 mg) was recovered from the first chromatography fraction. A second fraction was collected, concentrated in vacuo, and the residue was recrystallized from EtOAc-hexane. Pure **5** (102 mg, 53%) was thereby obtained as a colorless microcrystalline solid: mp 218-219 °C; IR (KBr) 3430 (s), 1680-1750 cm^{-1} (br, s); ^1H NMR ($CDCl_3$) δ 0.00 (s, 10 H), 2.05 (br s, 1 H), 2.72 (m, 1 H), 3.2 (br s, 1 H), 3.18 (t, J = 3.0 Hz, 1 H), 3.64 (s, 3 H), 3.66 (s, 3 H), 3.75 (s, 3 H), 3.76 (s, 3 H), 3.85 (s, 3 H), 3.85 (s, 3 H), 4.34 (s, 1 H), 4.63 (dd, J_1 = 9.0 Hz, J_2= 3.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ -1.60 (q), 35.32 (d), 45.44 (d), 46.27 (d), 49.94 (s), 51.25 (d), 52.62 (q), 52.75 (q), 52.02 (q), 52.18 (q), 53.38 (q), 53.70 (d), 54.30 (s), 54.36 (s), 54.72 (s), 56.28 (s), 72.70 (s), 78.97 (d), 137.55 (s), 138.66 (s), 163.32 (s), 164.13 (s), 164.43 (s), 164.70 (s), 166.80 (s), 167.04 (s), 171.38 (s), 191.38 (s). Anal. Calcd for $C_{30}H_{34}O_{16}Si$: C, 53.09; H, 5.05. Found: C, 53.16; H, 5.12.

Method B. To a solution of **3** (100 mg, 0.141 mmol) in CH_2Cl_2 (5 mL) and MeOH (2 mL) was added silica gel (200-400 mesh, 1 g). The resulting mixture was carefully concentrated in vacuo, and the residue was allowed to stand under ambient conditions, in contact with atmospheric moisture, for 3 days. The reaction mixture then was purified by column chromatography on silica gel by using 40% EtOAc-hexane as eluent. The eluate was recrystallized from methanol, thereby affording pure **6** as a colorless microcrystalline solid: mp 224-225 °C; IR (KBr) 3007 (w), 2951 (w), 1771-1700 (br, vs), 1647 (w), 1429 (m), 1316 (m), 1302 (m), 1253 (m), 1196 (m), 1147 (m), 836 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 0.082 (s, 9 H), 1.18 (d, J = 1.85 Hz, 1 H), 2.63 (dd, J_1 = 7.0 Hz, J_2 = 5.9 Hz, 1 H), 3.32 (t, J = 2.0 Hz, 1 H), 3.55 (dd, J_1 = 4.8 Hz, J_2 = 2.6 Hz, 1 H), 3.62 (s, 3 H), 3.63 (s, 3 H), 3.69 (s, 3 H), 3.74 (s, 3 H), 3.78 (s, 3 H), 3.86 (s, 3 H), 3.93 (s, 3 H), 4.35 (s, 1 H), 4.45 (dd, J_1 = 8.3 Hz, J_2 = 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ -1.38 (q), 37.06 (d), 46.91 (s), 49.02 (d), 49.24 (d), 52.23 (q), 52.28 (q), 52.67 (q), 52.73 (q), 53.19 (d), 53.24 (d), 53.94 (q), 55.50 (s), 55.94 (q), 55.98 (q), 57.77 (s), 58.55 (s), 80.63 (d), 82.17 (s), 113.80 (s), 131.83 (s), 153.82 (s), 159.75 (s), 163.23 (s), 164.57 (s), 164.90 (s), 167.34 (s), 167.73 (s), 167.85 (s). Anal. Calcd for $C_{31}H_{36}O_{16}Si$: C, 53.75; H, 5.24. Found: C, 53.79; H, 5.28.

Diels-Alder Cycloaddition of Cyclopentadiene to DMAD Tetramer (1). A solution of cyclopentadiene (freshly cracked from dicyclopentadiene,[11] 0.33 g, 5 mmol, excess) in dry benzene (4 mL) was cooled externally to 0-5 °C and stirred rapidly. To this cooled solution was added **1** (0.40 g, 0.70 mmol). The reaction mixture was stirred at 5 °C for 1 h and then placed in a refrigerator at 5-10 °C for 3 days. Hexane (20 mL) was added, whereupon a colorless solid

precipitated. The precipitate was collected via suction filtration. The residue was purified via column chromatography on silica gel by eluting with 1:1 EtOAc-hexane. Pure **4** (300 mg, 67%) was thereby obtained as a colorless microcrystalline solid: mp 202-203 °C; IR (KBr) 3008 (w), 2944 (w), 2850 (w), 1763-1715 (br, vs), 1636 (w), 1448 (m), 1324 (s), 1288 (s), 1259 (s), 1216 (s), 1197 (m), 1160 (m), 1153 (m), 1090 (m), 1040 (w), 980 cm^{-1} (w); ^1H NMR ($CDCl_3$) d 1.60 (δ *AB*, J_{AB} = 10.5 Hz, 1 H), 2.03 (A*B*, J_{AB} = 10.5 Hz, 1 H), 2.37 (dd, J_1 = 8.1 Hz, J_2 = 4.5 Hz, 1 H), 3.21 (m, 1 H), 3.42 (m, 1 H), 3.55 (s, 3 H), 3.57 (s, 3 H), 3.60 (s, 3 H), 3.65 (s, 3 H), 3.73 (s, 3 H), 3.76 (s, 3 H), 3.82 (s, 3 H), 3.88 (s, 3 H), 4.37 (dd, J_1 = 8.5 Hz, J_2 = 3.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 41.20 (t), 43.14 (d), 44.77 (s), 46.62 (d), 48.89 (s), 52.08 (d), 52.42 (3 C, q), 52.95 (q), 53.17 (q), 54.13 (q), 55.29 (s), 55.48 (q), 56.04 (q), 59.94 (s), 82.18 (d), 82.91 (s), 88.92 (s), 114.00 (s), 133.45 (s), 153.55 (s), 154.89 (s), 160.56 (s), 164.03 (s), 165.64 (s), 165.95 (s), 167.79 (s), 168.14 (s). Anal. Calcd for $C_{29}H_{30}O_{16}$: C, 54.73; H, 5.09. Found: C, 54.84; H, 5.05.

Acidic Hydrolysis of 4. Method B. The procedure described above for acidic hydrolysis of **3** (Method B) was used to hydrolyze **4** (100 mg, 0.141 mmol). The crude product was purified by column chromatography on silica gel by using 35-40% EtOAc-hexane as eluent. The eluate was recrystallized from methanol, thereby affording pure **7** as a colorless microcrystalline solid: mp 202-203 °C, mixture mp of a 1:1 mixture of **7** and **4**: mp 185-190 °C; IR (KBr) 3040 (w), 2976 (m), 2912 (w), 2864 (w), 1774-1710 (br, vs), 1652 (w), 1539 (w), 1453 (m), 1333 (s), 1330 (s), 1280 (s), 1189 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 1.71 (*AB*, *J* = 12.6 Hz, 1 H), 2.15 (A*B*, *J* = 12.6 Hz, 1 H), 2.66-2.78 (m, 1 H), 3.30 (m, 1 H), 3.51-3.59 (m, 1 H), 3.60 (s, 3 H), 3.62 (s, 3 H), 3.69 (s, 3 H), 3.74 (s, 3 H), 3.77 (s, 3 H), 3.85 (s, 3 H), 3.93 (s, 3 H), 4.33 (s, 1 H), 4.41 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 37.35 (d), 43.52 (s), 42.82 (t), 45.53 (d), 49.29 (d), 51.25 (d), 52.33 (q), 52.79 (q), 52.82 (q), 52.88 (q), 53.29 (q), 53.33 (q), 54.84 (s), 44.88 (s), 55.95 (q), 57.55 (s), 80.95 (d), 82.45 (s), 113.77 (s), 132.00 (s), 153.88 (s), 159.88 (s), 163.34 (s), 164.63 (s), 164.99 (s), 167.15 (s), 167.55 (s), 167.64 (s); Anal. Calcd for C_{28} H_{28} O_{16}: C, 54.20; H, 4.55. Found: C, 54.25; H, 4.27.

X-ray Crystal Structures of 3, 5, and 6.[12] X-ray data were collected on two Rigaku AFC6S diffractometers by using monochromated Cu Kα radiation for **3** and **6** and Mo Kα radiation for **5**. The ω-2θ scan technique was used to obtain X-ray data for all three compounds. Compound **3**: Space group $P2_1/c$; a = 16.034 (5), b = 12.444 (8), c = 17.010 (6) Å, β = 90.67 (3)°; V = 3394 (4) $Å^3$; D_c = 1.383 $g\text{-}cm^{-3}$; R = 0.076, Rw = 0.077 for 463 variables and 2662 reflections with $I>3\sigma(I)$. Compound **5**: Space group $P2_1/a$; a = 8.302 (4), b = 23.519 (6), c = 16.981 (4) Å, β = 103.05°; V = 3230 (4) $Å^3$; D_c = 1.457 $g\text{-}cm^3$; R = 0.170 for 3605 reflections with $I>3\sigma(I)$. The trimethylsilyl group and several methyl groups are disordered. After

the structure was confirmed, no further refinement was attempted. Compound **6**: Space group $P2_1/n$; a = 13.218 (2), b = 12.085 (2), c = 20.594 (1) Å, β = 98.926 (8)°; V = 3249.6 (7) $Å^3$; D_c = 1.416 g-cm^{-3}; R = 0.058, Rw = 0.058 for 458 variables and 3782 reflections with $I>3\sigma(I)$.

Acknowledgment. We thank the Robert A. Welch Foundation (Grant B-963 to A. P. M., Grant P-074 to W. H. W.) for financial support of this study.Helpful discussions with Professor Ian Fleming are gratefully acknowledged.

References & Footnotes

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12. Tables of atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, H-atoms coordinates, and isotropic thermal parameters (47 pages) for **3**, **5**, and **6** are available upon request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CV2 1EW, U. K. Requests should be accompanied by the full literature citation for this article.