Stereoselective photodimerisation of chalcones in the molten state

Fumio Toda,[*,a] **Koichi Tanaka**[a] **and Masako Kato,**[*,b]

[a] *Department of Applied Chemistry, Faculty of Engineering, Ehime University, Matsuyama, Ehime 790, Japan*
[b] *Department of Chemistry, Faculty of Science, Nara Women's University, Nara, Nara 630, Japan*

Photodimerisations of chalcone and its derivatives in the molten state proceed efficiently and stereoselectively to give *rac-anti*-head-to-head dimers in all cases tested.

Introduction

Although photodimerisations of chalcone and its derivatives in solution have long been studied, most gave unsatisfactory results. For example, irradiation of chalcone **1a**[1] and 4′-methylchalcone **1b**[2] in solution gave the corresponding *anti*-head-to-head dimers **5a** and **5b**, respectively, in very poor yield.[3] Photodimerisation of chalcones **1** in the solid state has also long been studied in order to correlate crystal-packing geometry with photochemical behaviour.[4] In spite of many efforts at photodimerisation by several research groups, all such attempts have failed except for one uncertain dimerisation experiment on 4-methoxychalcone **1d**[5] in the solid state which gave a mixture containing *syn*-head-to-head dimer **2d**.[3] X-Ray analysis of compound **1d** as a crystal showed that the shortest contact of C=C groups of two neighbouring **1d** molecules is 4.2 Å. In all other photochemically inert chalcones, the shortest contacts are longer than 4.2 Å. Finally, the rule 'the photodimerisation of chalcone occurs when the distance between C=C groups is shorter than 4.2 Å', the so-called Schmidt's rule, has appeared.[6] However, in an inclusion crystal of chalcone **1a** with 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol host compound **3**,[7] **1a** molecules aggregate in close positions and give product **4a** in 90% yield by photoirradiation in the solid state.[7,8]

a; Ar = Ar' = Ph

b; Ar = Ph, Ar' = —⟨ ⟩—Me

c; Ar = Ph, Ar' = —⟨ ⟩—Cl

d; Ar = —⟨ ⟩—OMe, Ar' = Ph

e; Ar = Ar' = —⟨ ⟩—Me

Results and discussion

We found that photodimerisations of chalcone and its derivatives proceed efficiently and stereoselectively in the molten state and give the corresponding *rac-anti*-head-to-head dimers **5** in relatively good yields. Irradiation of one polymorphic crystal of chalcone **1a** (form II, mp 56 °C)[9] (1 g) at 60 °C for 24 h by a 400 W high-pressure Hg lamp gave, after recrystallisation from MeOH, compound **5a** as prisms (0.31 g, 31%; mp 123–125 °C). Similar irradiation of another polymorphic crystal form of chalcone **1a** (form I, mp 59 °C)[10] at 60 °C also gave compound **5a** in 28% yield. This is a very efficient photodimerisation method, because neither form I nor form II of chalcone **1a** gives any dimer by photoirradiation in the solid state.[9,10] The structure of product **5a** was elucidated from its ¹H NMR spectrum which shows highly shielded CH proton signals at δ 3.97 and 4.61. The structure was finally determined by X-ray analysis (Fig. 1). Although X-ray data for compound **5a** have already been reported,[11] we used our own data, because of its improved quality. Dimer **5a** has been prepared so far in 9% yield as a crystal (mp 124 °C) by photoirradiation of chalcone **1a** in EtOH for 147 h, and the structure has been estimated by a chemical method.[2] Similar irradiation of compound **1b** (1 g, mp 74–75 °C) at 80 °C for 24 h gave, after recrystallisation from MeOH, dimer **5b** as prisms (0.27 g, 27%; mp 112–114 °C). By comparison of its ¹H NMR spectrum with that of dimer **5a**, the structure of compound **5b** was determined. By prolonged irradiation of compound **1b** in EtOH for 16 days, a mixture of its two kinds of dimers, mps 114 and 218 °C, has been obtained in 45% yield.[9] The former product would be identical with dimer **5b**. Similarly, irradiation of chalcones **1c** (mp 96–98 °C),[11] **1d** (mp 74 °C)[5] and **1e** (mp 127 °C)[12] in their molten state gave the corresponding *rac-anti*-head-to-head dimers **5c** (25% yield; mp 128–129 °C), **5d** (20% yield; mp 90–92 °C) and **5e** (32% yield; mp 137–139 °C), respectively, in the yields indicated. Structures of compounds **5c–e** were elucidated by comparison of their ¹H NMR spectra with that of the parent dimer **5a**.

All photodimerisations of chalcones **1a–e** in the molten state gave *rac-anti*-head-to-head dimers **5a–e**. This result suggests that two molecules of chalcone **1** aggregate in the liquid state so as to give the dimer **5** by photoreaction as shown in structure **6**. Since irradiation of substrates **1a** and **1b** in solution also gives dimers **5a** and **5b**, respectively, in low yields,[2] molecules of chalcone **1** would also be relatively easy to aggregate as species **6** even in solution. The aggregation of dimers **5a–e** as species **6** would be energetically the most favourable. Since photodimerisation of chalcones **1** is more efficient in the molten state than in solution, molecules of substrate **1** would more easily aggregate as structures **6** in the molten state. In solution, solvent molecules probably interrupt the molecular aggregation of chalcones **1**.
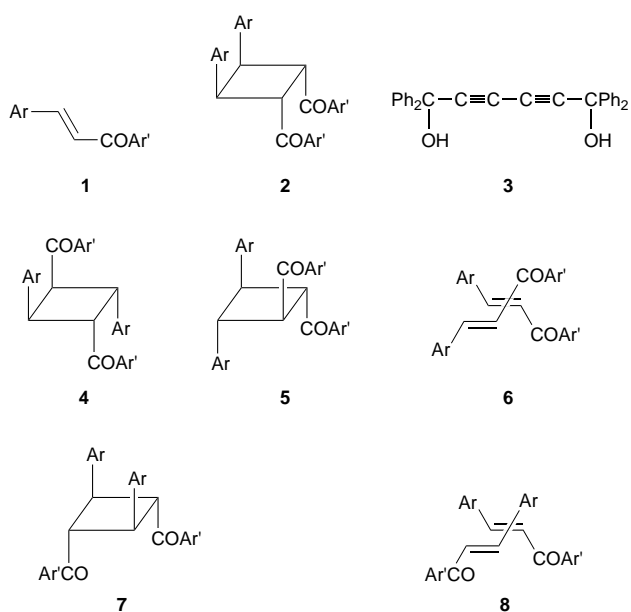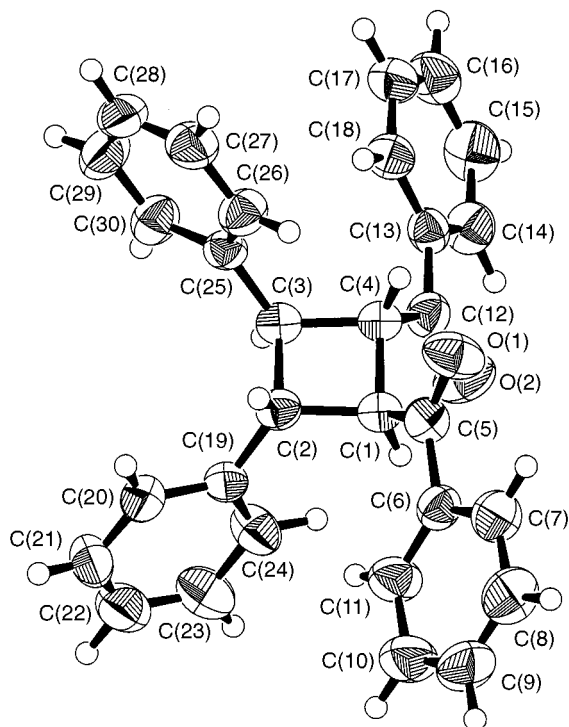
Fig. 1 Molecular structure of dimer **5a** with crystallographic numbering scheme. Selected bond lengths (Å) and angles (°): O(1)–C(5) = 1.219(3), O(2)–C(12) = 1.216(3), C(1)–C(2) = 1.568(3), C(1)–C(4) = 1.541(3), C(1)–C(5) = 1.509(3), C(2)–C(3) = 1.567(3), C(2)–C(19) = 1.507(3), C(3)–C(4) = 1.563(3), C(3)–C(25) = 1.502(3), C(4)–C(12) = 1.509(3), C(5)–C(6) = 1.488(3), C(12)–C(13) = 1.496(3); C(2)–C(1)–C(4) = 90.0(2), C(2)–C(1)–C(5) = 116.1(2), C(4)–C(1)–C(5) = 116.2(2), C(1)–C(2)–C(3) = 89.4(2), C(1)–C(2)–C(19) = 120.1(2), C(3)–C(2)–C(19) = 114.7(2), C(2)–C(3)–C(4) = 89.2(2), C(2)–C(3)–C(25) = 116.8(2).

All of the molecules of chalcones **1a**–**e** aggregate similarly in their molten state as discussed above. However, molecules of chalcones **1** in crystals do not aggregate in a definite manner. The crystal structure of 4-methoxychalcone **1d** (mp 74 °C)[5] has been shown by X-ray analysis to have a molecular aggregation with 4.2 Å shortest C=C contact, which should give *syn*-head-to-head dimer **2d** by photodimerisation.[3] On the other hand, molecules of 4′-chlorochalcone **1c** were found to be arranged in the crystal in a different manner from that of analogue **1d**. Irradiation of powdered compound **1c**[12] (1 g) in a stirred water suspension containing a small amount of hexadecyl(trimethyl)ammonium bromide as a surfactant for 12 h by 100 W high-pressure Hg-lamp gave *syn*-head-to-tail dimer **4c** as prisms, after recrystallisation from AcOEt (0.31 g, 31%; mp 255–257 °C). An X-ray analysis showed that two **1c** molecules are aggregated at 4.238 Å shortest C=C contact in the positions which give the **4c** dimer by photoreaction (Fig. 2). However, 4′-methylchalcone **1b** molecules are arranged in the same way as are the **1c** substrate molecules, although C=C contact is too long, 4.5 Å, to dimerise in the solid state (Fig. 3). Chiral order of 4,4′-dimethylchalcone molecules **1e**[13] in their crystal state has been elucidated by X-ray analysis.[13] Enantioselective bromine addition to the chiral crystal of compound **1e** which gives the optically active bromine addition product in low optical yield has also been reported.[14] Although irradiation of the chiral crystal of compound **1e** was carried out in the solid state in the expectation of the formation of optically active photodimer, substrate **1e** was photochemically inert. This is very reasonable, because the C=C contact in the compound **1e** crystal is too long (5.9 Å) to react.[13] The chiral arrangement of compound **1e** molecules in the crystal was easily detected by measurement of CD spectra (Fig. 4) in Nujol mull.[15] In Fig. 4, a nice mirror-image relationship of two enantiomeric chiral crystals of **1e** is shown.
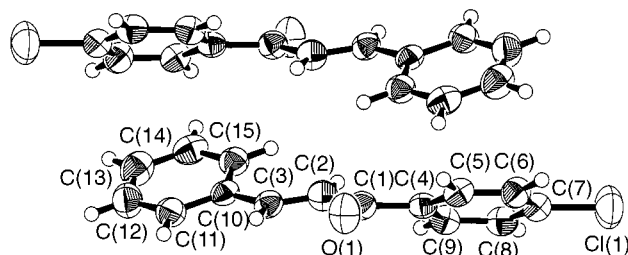
Fig. 2 Molecular structure of compound **1c** with crystallographic numbering scheme. Selected bond lengths (Å) and angles (°): C(1)–C(7) = 1.736(3), O(1)–C(1) = 1.227(3), C(1)–C(2) = 1.475(4), C(1)–C(4) = 1.492(4), C(2)–C(3) = 1.323(4), C(3)–C(10) = 1.455(4); O(1)–C(1)–C(2) = 121.4(2), O(1)–C(1)–C(4) = 119.5(2), C(2)–C(1)–C(4) = 119.1(2), C(1)–C(2)–C(3) = 121.7(3), C(2)–C(3)–C(10) = 128.0(3). Non-bonded contacts (Å): C(2)···C(2′) = 4.002(4), C(3)···C(3′) = 4.840(4) and C(2)···C(3′) = 4.239(4) (′ = 1 − x, −y, 1 − z).
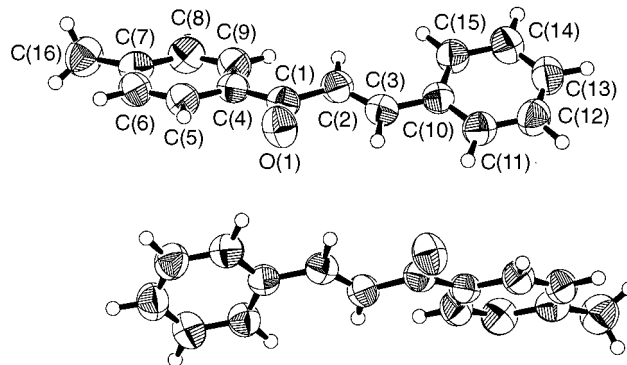

Fig. 3 Molecular structure of compound **1b** with crystallographic numbering scheme. Selected bond lengths (Å) and angles (°): O(1)–C(1) = 1.229(2), C(1)–C(2) = 1.478(2), C(1)–C(4) = 1.488(2), C(2)–C(3) = 1.321(2), C(3)–C(10) = 1.463(2); O(1)–C(1)–C(2) = 120.0(2), O(1)–C(1)–C(4) = 119.9(1), C(2)–C(1)–C(4) = 120.2(1), C(1)–C(2)–C(3) = 121.0(2), C(2)–C(3)–C(10) = 128.4(2). Non-bonded contacts (Å): C(2)···C(2′) = 5.053(2), C(3)···C(3′) = 4.162(2) and C(2)···C(3′) = 4.502(2) (′ = 1 − x, y, 3/2 − z).
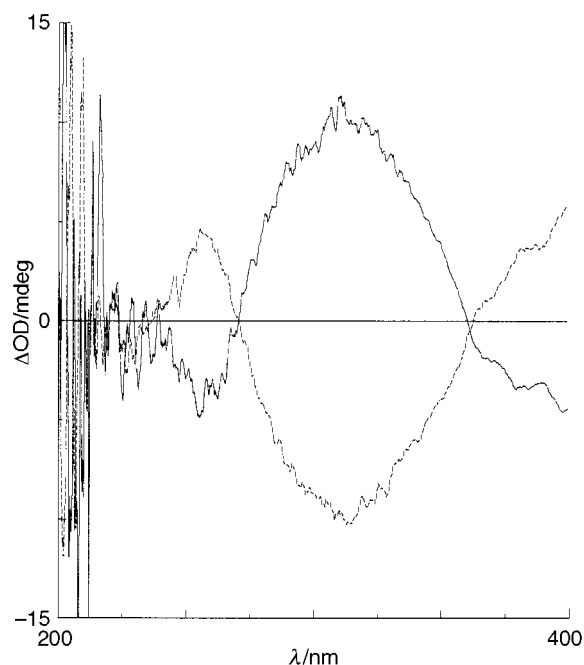

Fig. 4 CD Spectra of two enantiomeric chiral crystals of compound **1e** in Nujol mulls

Of the four possible dimers of chalcones **1**, three of them, compounds **2**, **4** and **5**, were isolated and their structures were elucidated completely. Since the *syn*-head-to-tail dimer structure of **4** has never been elucidated directly so far, the X-ray
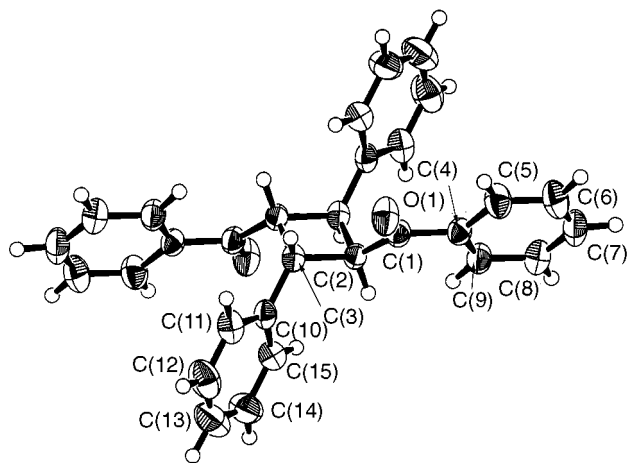
Fig. 5 Molecular structure of dimer **4a** with crystallographic numbering scheme. Selected bond lengths (Å) and angles (°): O(1)–C(1) = 1.212(2), C(1)–C(2) = 1.512(2), C(1)–C(4) = 1.500(2), C(2)–C(3) = 1.551(2), C(2)–C(3′) = 1.586(3), C(3)–C(10) = 1.504(3); O(1)–C(1)–C(2) = 121.5(2), O(1)–C(1)–C(4) = 120.4(2), C(2)–C(1)–C(4) = 118.1(2), C(1)–C(2)–C(3) = 116.1(1), C(1)–C(2)–C(3′) = 115.9(1), C(3)–C(2)–C(3′) = 91.3(1), C(2)–C(3)–C(2′) = 88.7(1), C(2)–C(3)–C(10) = 117.5(1), C(2′)–C(3)–C(10) = 118.3(1). The equivalent position ′ = −x, −y, 2 − z.

structure of compound **4a** prepared according to the literature[7] was determined (Fig. 5). However, no *anti*-head-to-tail dimer **7** was detected in any of the photodimerisation experiments which have been carried out so far. This shows that the molecular aggregation such as **8** which gives dimer **7** by photodimerisation would be unfavourable. It is also clarified that mps of chalcone photodimers become higher in the sequence: **4** (232–257 °C) > **2** (164 °C) > **5** (90–139 °C).

Experimental

Mps were measured on a Yanaco MP-53 apparatus and are uncorrected. ^{1}H NMR spectra were recorded in CDCl$_3$ by a JEOL LA-300 300 MHz spectrometer. *J*-Values are given in Hz. IR spectra were recorded on a JASCO FT-IR spectrophotometer for samples as Nujol mulls.

Photodimerisation of compound 1a in the molten state
Chalcone **1a** (1 g, 4.8 mmol) was placed in between two Pyrex glass plates and the sample was melted by being heated at 60 °C on a hot-plate, and thereafter was irradiated with a 400 W high-pressure Hg lamp for 24 h. The oily crude product was crystallised by addition of a small amount of MeOH to give, after recrystallisation from MeOH, *compound* **5a** as prisms (0.31 g, 31%), mp 123–125 °C; v_{max}(C=O) 1665 cm^{-1}; δ_H 7.8–7.1 (20 H, m, ArH) and 4.61 and 3.97 (2 H, each d, *J* 8.8, CH) (Found: C, 86.39; H, 5.88. C$_{30}$H$_{24}$O$_2$ requires C, 86.51; H, 5.81%).

Photodimerisation of compound 1b in the molten state
By a similar method to that above, chalcone **1b** (1 g, 4.5 mmol) was irradiated in the molten state for 24 h to give, after recrystallisation from MeOH, *compound* **5b** as prisms (0.27 g, 27%), mp 112–114 °C (lit.,[2] 114 °C); v_{max}(C=O) 1665 cm^{-1}; δ_H 7.7–7.1 (18 H, m, ArH), 4.57 and 3.95 (2 H, each d, *J* 9.0, CH) and 2.32 (6 H, s, CH$_3$).

Photodimerisation of compound 1c in the molten state
By a similar method to that above, chalcone **1c** (1 g, 4.1 mmol) was irradiated in the molten state for 24 h to give, after recrystallisation from MeOH, *compound* **5c** (0.25 g, 25%), mp 128–129 °C; v_{max}(C=O) 1660 cm^{-1}; δ_H 7.8–7.2 (18 H, m, ArH) and 4.54 and 3.90 (2 H, each d, *J* 9, CH) (Found: C, 74.02; H, 4.33. C$_{30}$H$_{22}$Cl$_2$O$_2$ requires C, 74.23; H, 4.57%).

Photodimerisation of compound 1d in the molten state
By a similar method to that above, chalcone **1d** (1 g, 4.2 mmol) was irradiated in the molten state for 24 h to give, after recrystallisation from MeOH, *compound* **5d** as needles (0.2 g, 20%), mp 90–92 °C; v_{max}(C=O) 1665 cm^{-1}; δ_H 7.8–7.1 (18 H, m, ArH), 4.58 and 3.88 (2 H, each d, *J* 9.0, CH) and 2.31 (6 H, s, OCH$_3$) (Found: C, 80.50; H, 5.63. C$_{32}$H$_{28}$O$_4$ requires C, 80.65; H, 5.92%).

Photodimerisation of compound 1c in the solid state
A stirred suspension of powdered chalcone **1c** (1 g, 4.1 mmol) in water (100 ml) containing a small amount of hexadecyl-(trimethyl)ammonium bromide as a surfactant was irradiated for 12 h at room temp. The reaction mixture was filtered and recrystallised from AcOEt to give *compound* **4c** as prisms (0.31 g, 31%), mp 255–257 °C; v_{max}(C=O) 1670 cm^{-1}; δ_H 7.7–7.0 (18 H, m, ArH) and 4.94 and 4.75 (2 H, each dd, J_{cis} 10.8, J_{trans} 6.4, CH) (Found: C, 74.13; H, 4.52. C$_{30}$H$_{22}$Cl$_2$O$_2$ requires C, 74.23; H, 4.57%).

Photodimerisation of compound 1e in the molten state
By a similar method to that above, chalcone **1e** (1 g, 4.2 mmol) was irradiated in the molten state for 24 h to give, after recrystallisation from MeOH, *compound* **5e** as prisms (0.32 g, 32%), mp 137–139 °C; v_{max}(C=O) 1660 cm^{-1}; δ_H 7.7–7.1 (16 H, m, ArH), 4.54 and 3.86 (2 H, each d, *J* 9, CH) and 2.32 and 2.31 (6 H, each s, CH$_3$) (Found: C, 86.17; H, 6.39. C$_{34}$H$_{32}$O$_2$ requires C, 86.41; H, 6.82%).

X-Ray crystal structure analysis
Crystal data for compound 4a. C$_{30}$H$_{24}$O$_2$, M = 416.52, triclinic, space group P1, *a* = 8.717(3), *b* = 11.863(4), *c* = 6.105(2) Å, α = 99.67(3)°, β = 105.53(2)°, γ = 107.73(3)°, V = 557.5(4) Å^3, Z = 1, D$_c$ = 1.24 g cm^{-3}, crystal dimensions 0.38 × 0.38 × 0.20 mm, μ(Mo-Kα) = 0.76 cm^{-1}. Diffraction data were collected on a Rigaku AFC-7R diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.710 73 Å) to 2θ_{max} = 55°. Intensity data were corrected for Lorentz and polarisation effects. All calculations were carried out using the TEXSAN crystallographic software package from Molecular Structure Corporation. Non-hydrogen and hydrogen atoms were refined anisotropically and isotropically, respectively. The final cycle of full-matrix least-squares refinement was based on 1530 observed reflections [I > 3σ(I)] and 194 parameters and converged with R = 0.046, R$_w$ = 0.060 ($w = [\sigma^2 (F_o) + 0.0009F_o{}^2]$), and GOF = 1.44; $\Delta\rho_{max}$ = 0.23 e Å^{-3}.

Crystal data for compound 5a. C$_{30}$H$_{24}$O$_2$, M = 416.52, monoclinic, space group P2$_1$/c, *a* = 10.905(2), *b* = 9.672(2), *c* = 21.406(2) Å, β = 90.79(1)°, V = 2257.5(5) Å^3, Z = 4, D$_c$ = 1.225 g cm^{-3}, crystal dimensions 0.32 × 0.32 × 0.20 mm, μ(Mo-Kα) = 0.75 cm^{-1}. Data collection and structure analysis were performed by the same method as described for compound **4a**. R = 0.039, R$_w$ = 0.058, GOF = 1.31 for 2465 observed reflections [I > 3σ(I)] and 386 parameters; $\Delta\rho_{max}$ = 0.14 e Å^{-3}.

Crystal data for compound 1b. C$_{16}$H$_{14}$O, M = 222.29, monoclinic, space group C2/c, *a* = 14.976(4), *b* = 9.843(3), *c* = 17.561(3) Å, β = 105.83(2)°, V = 2490(1) Å^3, Z = 8, D$_c$ = 1.186 g cm^{-3}, crystal dimensions 0.60 × 0.50 × 0.53 mm, μ(Mo-Kα) = 0.72 cm^{-1}. Data collection and structure analysis were performed by the same method as described for compound **4a**. R = 0.042, R$_w$ = 0.054, GOF = 2.83 for 1915 observed reflections [I > 3σ(I)] and 155 parameters; $\Delta\rho_{max}$ = 0.15 e Å^{-3}.

Crystal data for compound 1c. C$_{15}$H$_{11}$ClO, M = 242.70, triclinic, space group P1, *a* = 7.565(2), *b* = 14.060(2), *c* = 5.858(1) Å, α = 90.09(2)°, β = 92.15(2)°, γ = 81.70(2)°, V = 616.0(3) Å^3, Z = 2, D$_c$ = 1.308 g cm^{-3}, crystal dimensions 0.30 × 0.14 × 0.14 mm, μ(Mo-Kα) = 2.88 cm^{-1}. Data collection and structure analysis were performed by the same method as described for compound **4a**. R = 0.034, R$_w$ = 0.049, GOF = 1.11 for 1241

observed reflections $[I > 3\sigma(I)]$ and 199 parameters; $\Delta\rho_{max} = 0.13$ e Å^{-3}.

Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/186.

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