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Photocycloaddition of chalcones to yield cyclobutyl ditopic cyclophanes

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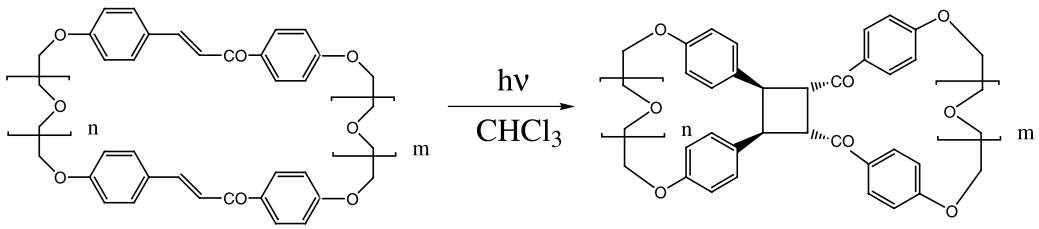
Abstract—The intramolecular photocycloaddition of chalcones to give cyclobutanes has proved to be a fast and convenient method to shrink a cyclophane ring to a tricyclic system, in order to prepare potential ditopic receptors. X-Ray results confirm the previously indicated structure for the cyclobutanes **2a** (n=1, m=1), in which the cyclization occurs by a head-to-head *syn* ring closure. NMR results indicate that the same process occurs for the cyclobutanes **2b** (n=2, m=2) and **2c** (n=1, m=3).

1. Introduction

In a previous paper we showed that in chloroform solution the chalcone **1a** photocyclises intramolecularly to the cyclobutane **2a**, by a fast and high yield process, that occurs by a head-to-head *syn* ring closure (Scheme 1).[1]

Since the size of the spacer could affect to some extent the stereochemical route of these processes, herein we wish to report on the effect that an enlargement of the spacer has on the intramolecular photocycloaddition of the chalcones **1b** and **1c** in chloroform. X-Ray results regarding the structures of the three chalcones **1a**–**1c** and the cyclobutane **2a** are also reported.

The formation of different stereoisomers in the dimerization of chalcones and related compounds may be dependent on the physical state of the substrate (solid, solution, molten state, glass)[2–9] or its complexation with Lewis acids.[10] The occurrence in solution of only one type of regiochemical (head-to-head or head-to-tail ring closure) and stereochemical ring closure, has already been observed with cyclic *trans*-cynnamoyl precursors, that give the formation of a *syn* head-to-head truxinic type cyclobutane (Fig. 1).[11,12]



1a n = 1 m = 1
1b n = 2 m = 2
1c n = 1 m = 3

2a n = 1 m = 1
2b n = 2 m = 2
2c n = 1 m = 3

Scheme 1.

Keywords: cyclophanes; enones; chalcones; carbocycles; cycloaddition; photochemistry; photocyclization.
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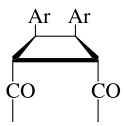


Figure 1.

A *syn* head-to-head ring closure was also observed in the photocycloadditions of *trans*-cinnamoyl derivatives, wherein the photoactive centers are linked to a phenylene ring in *ortho* relationship,[13] or to a [2.2]paracyclophane system in pseudo-geminal relationship.[14] In these cases a regiospecific ring closure is undoubtedly favoured by the structures of the precursors, that constrain the reactive centers in close proximity; nevertheless, this behaviour may also be observed in some photochemical ring closure processes of acyclic precursors, carried out in solution. For example, the cyclization of *trans*–*trans*-dibenzylideneacetone in benzene give only the *anti* head-to-head truxinic type cyclobutane as the photodimeric product (Fig. 2).[15]

Recently, a rationalization of the regiochemical and stereochemical behaviour of some photosensitized dimerizations, occurring in solution, has been offered.[16]

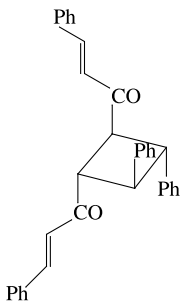
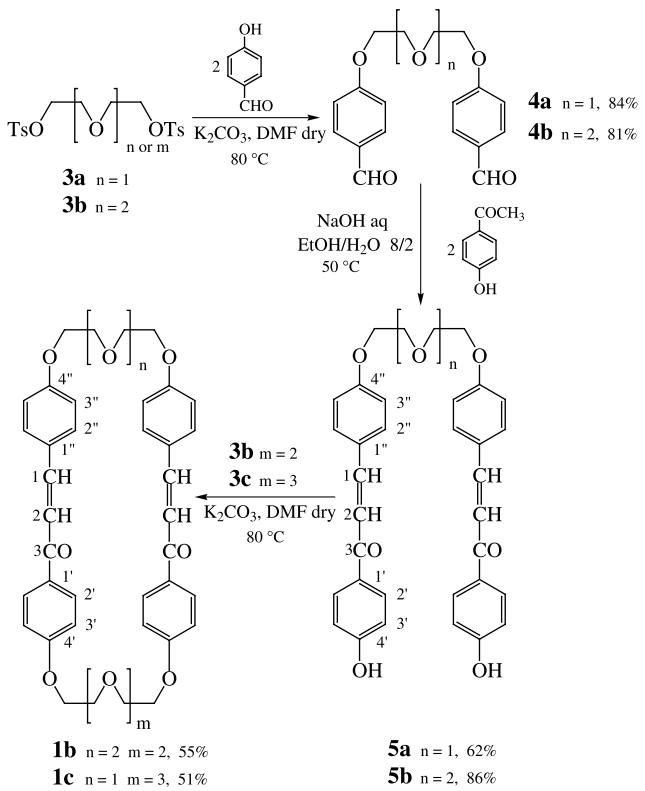


Figure 2.



Scheme 2.

2. Results and discussion

Chalcones **1b** and **1c** have been synthesized according to the route used for the synthesis of **1a** (Scheme 2).[†,1] These chalcones (3.3×10^{-3} mol dm^{-3} in chloroform), when exposed to sunlight, are converted to the respective cyclobutanes **2b** and **2c**, with yields (chromatographated products) of 68% (**2b**) and 71% (**2c**). Better yields are obtained when **1b** and **1c** are exposed to 14 350 nm centred lamps, in a Rayonet reactor. In this case cyclobutanes **2b** and **2c** are obtained with yields of 81 and 86%, respectively.

At variance with the experiments carried out in solution, the exposure to sunlight for 6 days of micro-crystals of **1a**–**1c**, obtained by slow evaporation of chloroform solutions, did not give any transformation of the substrates, which were recovered unchanged. X-Ray measurements support these findings because, in these crystals, the C=C double bonds are not parallel, with intramolecular distances (Fig. 3(a), (b) and (c)) that are greater than the reported limits for solid state photodimerizations (3.5–4.2 Å),[5] even though some exceptions have been reported.[17] On the other hand the intermolecular solid phase photocyclization is also not permitted, since the C=C distances between the nearest molecules are 4.1 Å (**1a**), 5.1 Å (**1b**) and 5.9 Å (**1c**).

In the crystals of **1a**–**1c** the conjugated C=O and C=C bonds are in the *s-cis* conformation, with dihedral angles ω varying from 9.4 to 15.2° for **1a**, from 5.6 to 11.1° for **1b**, and from 8.9 to 9.3° for **1c** (for comparison, in benzylideneacetophenone ω=16.9°).[18] The *s-cis* conformation is frequently observed in the chalcone derivatives, but some exceptions have been reported.[19] The dihedral angles of the O=C–C_{Ar}–C_{Ar} bonds are <29°, i.e. lower than 39° as generally observed for aromatic enones having only hydrogen atoms in *ortho* positions.[20]

After our previous work, we were able to obtain suitable crystals to carry out X-ray crystallographic analysis of the cyclobutane **2a** by a very slow evaporation of a chloroform solution. The results confirm unequivocally our previous conclusions regarding the structure of this compound (Fig. 4), obtained by NOESY measurements.[1] Nevertheless, since suitable crystals of **2b** and **2c** are not available to us for X-ray analysis, we have utilized the NMR measurements to determine their stereochemistry.

The structure of **2c** was elucidated by NOESY measurements. In fact, due to the short dioxyethylene spacer, this compound presents, like the cyclobutane **2a**,[1] restricted rotations of the phenylene rings directly bonded to the cyclobutane ring. As a consequence, both the *ortho* protons and carbons 2″a and 2″d, and the *meta* protons and carbons 3″b and 3″c (Fig. 5) are not chemically equivalents.

This feature enable us to distinguish the through-space

[†] Erratum: Scheme 2 of Ref. 1 shows an inverted numbering of the phenylene group bonded to the carbonyl group.

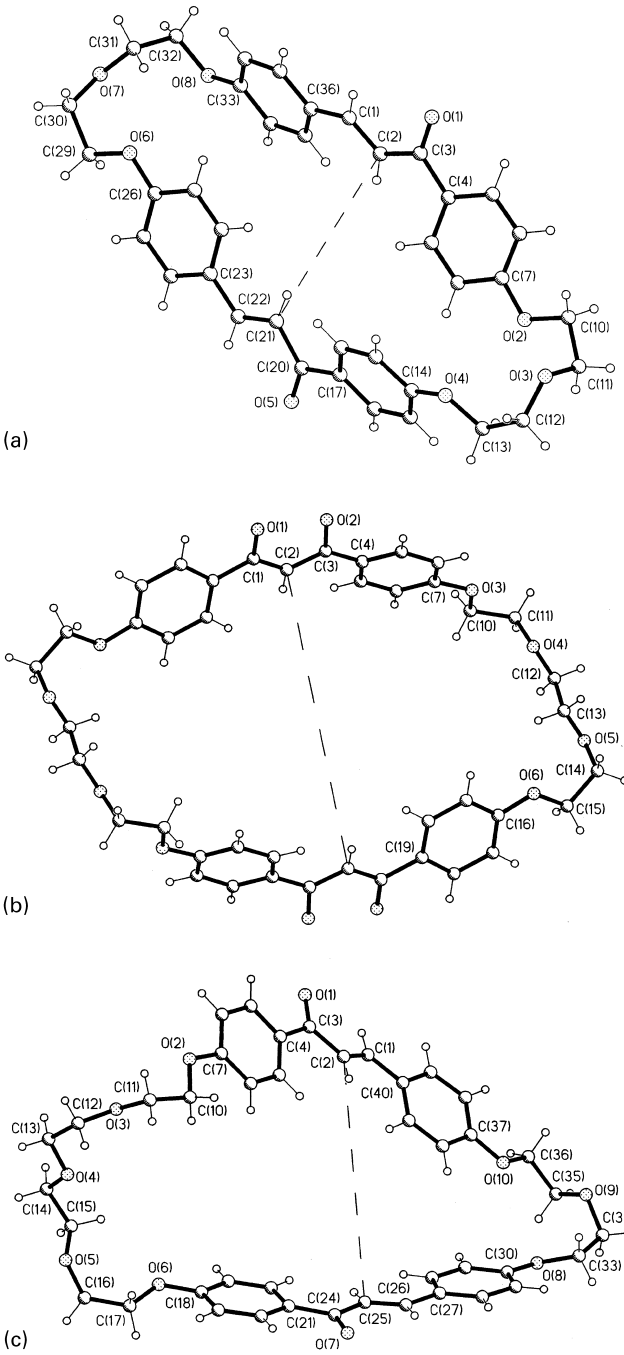


Figure 3. (a) A perspective view of the X-ray molecular structure of compound **1a**. The intramolecular distance of 5.6 Å (dashed line) is shown. Selected bond lengths (Å): O(1)–C(3) 1.22(1), O(5)–C(20) 1.23(1), C(1)–C(2) 1.335(8), C(21)–C(22) 1.32(1). (b) View of the centrosymmetric molecular structure of compound **1b**, showing the carbonylic oxygen atoms disordered on the two crystallographically non-equivalent, O(1) and O(2) positions. The intramolecular distance of 9.9 Å between the two centrosymmetrical ethylenic carbon atoms is shown (dashed line). Selected bond lengths (Å): O(1)–C(1) 1.33(2), C(1)–C(2) 1.39(2), C(2)–C(3) 1.40(2), O(2)–C(3) 1.31(2). (c) X-Ray molecular structure of compound **1c**. The intramolecular distance of 8.1 Å (dashed line) is shown. Selected bond lengths (Å): O(1)–C(3) 1.221(7), O(7)–C(24) 1.235(6), C(1)–C(2) 1.316(7), C(1)–C(40) 1.465(8), C(2)–C(3) 1.466(8), C(3)–C(4) 1.472(6), C(21)–C(24) 1.482(8), C(24)–C(25) 1.474(7), C(25)–C(26) 1.327(8), C(26)–C(27) 1.445(7).

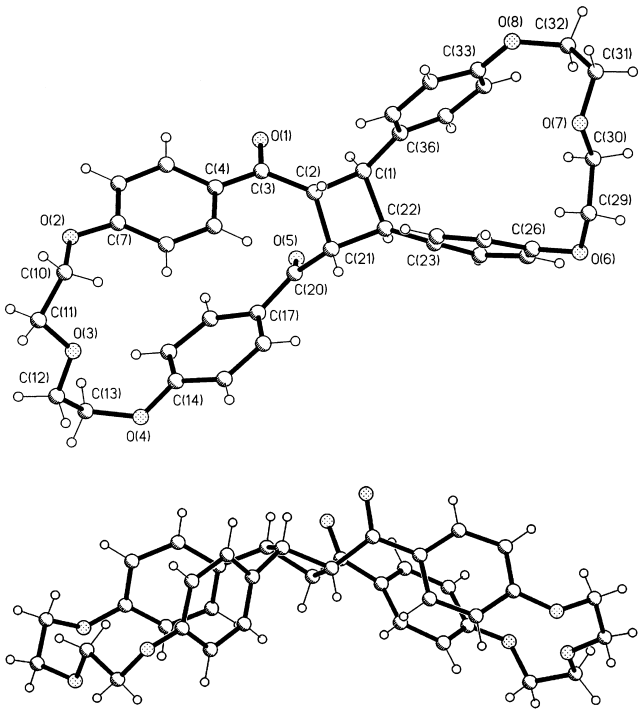


Figure 4. Two different perspective drawings of the molecular structure of compound **2a**, showing the labelling of the atoms (the upper one) and the **2h**–**h** *syn* conformation (the lower one). Selected bond lengths (Å): C(1)–C(2) 1.57(2), C(1)–C(22) 1.59(2), C(2)–C(21) 1.58(2), C(21)–C(22) 1.56(2).

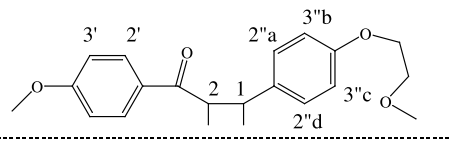


Figure 5.

interactions of proton 2″a from those of 2″d. In particular, the NOESY spectrum of **2c** shows that the protons that we have named H-2″a have a through-space coupling exclusively with the protons H-2, whereas the protons that

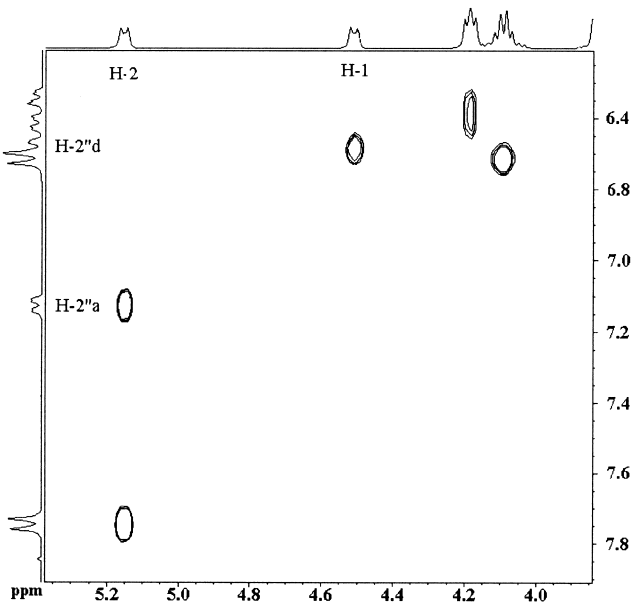


Figure 6. NOESY spectrum of **2c** (detail).

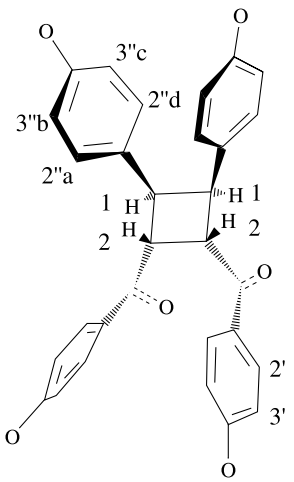


Figure 7. Head-to-head *syn* structure of **2c** (the dioxyethylene chains have been omitted).

we have named H-2″d couple through the space only with the protons H-1 (Fig. 6). These results, that are identical to those obtained for compound **2a**,[1] indicate that there is a *trans* relationship between protons H-1 and H-2, and a *cis* relationship between the two H-1 protons, caused by a head-to-head *syn* junction (Fig. 7).[21]

Owing to the larger dimensions of the trioxyethylene chains, in the cyclobutane **2b** we did not observe the restricted rotations of the phenylene rings directly bonded to the cyclobutane ring. Such restricted rotations, as stated previously, made the related *ortho* and *meta* protons of **2a** and **2c** not chemically equivalent, and were decisive in establishing the structures by NOESY. However, the comparison of ^{1}H NMR spectra of **2a**, **2c** and **2b** gave suggestions about the stereochemistry of the latter compound. Figure 8 shows the AA′BB′ patterns of cyclobutyl protons of **2a**, **2b** and **2c**, and Table 1 reports the calculated coupling constants for these systems.

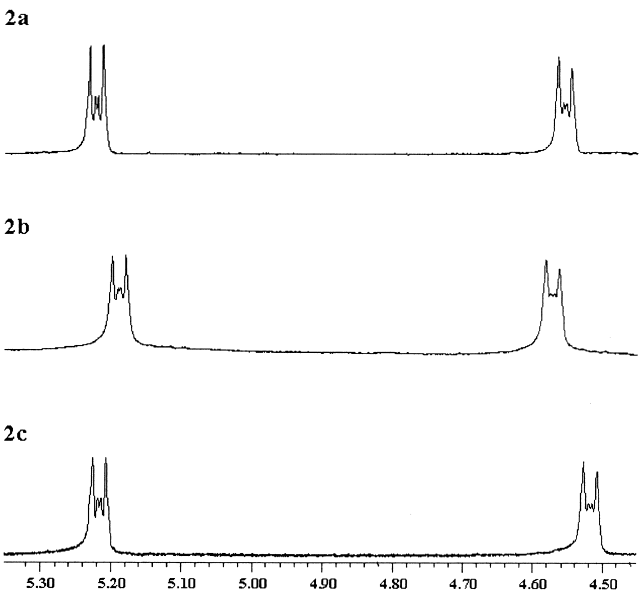


Figure 8. ^{1}H NMR spectra of cyclobutyl protons of **2a**, **2b** and **2c** in acetone-d_6, at 45°C.

Table 1. Calculated chemical shifts and coupling constants of the AA′BB′ cyclobutyl protons of **2a**–**2c**, in acetone-d_6[24]

Compound	δ *H*-1 (ppm)	δ *H*-2 (ppm)	$J_{AA'}$ (Hz)	J_{AB} (Hz)	$J_{AB'}$ (Hz)	$J_{BB'}$ (Hz)
2a	4.56	5.22	11.4	6.5	−0.7	10.1
2b	4.57	5.19	11.0	6.4	−0.8	10.0
2c	4.52	5.21	10.6	6.5	−0.9	9.8

Even though the values of these coupling constants should only indicate that the formation of the cyclobutane system occurs by a head-to-head coupling,[22,23] the close similarity of the ^{1}H NMR pattern of the cyclobutyl moieties strongly suggests that also for **2b** the formation of cyclobutane ring occurs by *syn* junction.

We have attempted to evaluate the differences of reactivity of the three chalcones **1a**–**1c**, by irradiation at 419 nm of diluted chloroform solutions ($\sim 10^{-6}$–10^{-5} mol dm^{-3}), kept at 25°C in a quartz cell into a Rayonet reactor,[25] and monitoring the progress of the reactions by UV–vis spectroscopy. These processes have shown the presence of isosbestic points, that suggest the absence of appreciable quantities of intermediates and/or by-products, at least at these low concentrations, and clean first order kinetics (Table 2). The ratios $k_{\mathbf{1a}}/k_{\mathbf{1b}}/k_{\mathbf{1c}}$=1.5:1.12:1, indicate a modest influence of the size of the polyoxyethylene chain.

Table 2. First order kinetic constants for the intramolecular photocyclization **1**→**2**, in chloroform at 25°C

Compound	k (s^{-1})
1a	$9.6\pm0.4\times10^{-3}$
1b	$7.2\pm0.7\times10^{-3}$
1c	$6.4\pm0.4\times10^{-3}$

3. Conclusions

X-Ray and NMR measurements confirm that the photocyclization of cyclic bis-chalcones **1** to give the corresponding cyclobutanes **2** is a process with a definite regiochemistry and stereochemistry. The *syn* relationship observed for the two carbonyl groups in the ditopic cyclophanes **2** is an important feature, because it could have implications on the potential ligand properties of these compounds, and could be exploited to construct more complex structures.

4. Experimental

4.1. General and instrumentation

Melting points were determined with a Büchi capillary instrument and are uncorrected. Thin-layer chromatography (TLC) was carried out on Merck precoated 60 Kiesegel F_{254} silica gel plates and Merck precoated RP-18 F_{254S} reverse phase plates. Flash chromatography was carried out on columns with flash silica gel 60 Merck (40–63 μm), or on Gyan prepacked flash silica gel columns (40–63 μm,

40 mm I.D.×75 mm) by a JaiFlash chromatograph. All reactions requiring anhydrous conditions were conducted in flame-dried apparatus. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker AC 200 or a Bruker AC 300 spectrometer, at 25°C unless otherwise specified. DEPT and 2D NMR spectra (H,H-COSY, H,C-COSY, NOESY-Phase sensitive) were measured using standard Bruker software. NOESY-Phase sensitive spectra in TPPI mode, were recorded with mixing-times of 100–400 ms. IS-MS spectra were obtained on a Perkin–Elmer SCIEX API 365 triple quadrupole spectrometer. UV–vis spectra were carried out on a Cary 300, at 25°C. IR spectra were recorded on an FT-IR Nicolet 510. Microanalyses were performed on a Carlo Erba EA 1110 CHNS-O analyser. Photoreactions were carried out in a Rayonet apparatus. X-Ray intensities were collected on a Rigaku four-circle diffractometer equipped with a rotating anode (Cu Kα radiation) by the $\theta-2\theta$ scan method. Data were corrected for Lorentz and polarization effects and for absorption by the semiempirical psi-scan method. The structures were solved by direct methods using the SIR2002 package of crystallographic programs,[26] and refined by full-matrix least-squares methods with the SHELXTL programs.[27] Hydrogen atoms were included in calculated positions and refined in riding mode.

4.2. Crystallographic data

The poor quality of the available, low diffracting crystals of **1a**, **1b** and **2a** strongly affects their crystal structure analysis and the geometrical results. Only for **1c**, which crystallizes as well formed prisms, diffraction data allowed to obtain a better molecular model, and interatomic distances and angles with low standard deviations.

Crystallographic data (excluding structure factors) for the strucures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 212952-212955.

4.2.1. Crystal structure of 1a. Crystal data: $C_{38}H_{36}O_8$, M=620.7, crystallizes as pale-yellow thin prisms; crystal dimensions 0.5×0.2×0.1 mm, triclinic, a=11.674(9), b=12.335(9), c=12.628(5) Å, α=106.52(4), β=94.88(4), γ=111.46(4)°, V=1585(5) Å^3, space group P-1, μ(Cu-Kα)=0.74 mm^{-1}, Z=2, d_{calc}=1.30 Mg m^{-3}, final conventional R=0.075 and R_w=0.090 for 2426 reflections with $F\geq6\sigma(F)$. Goodness of fit=2.29.

4.2.2. Crystal structure of 1b. Crystal data: $C_{21}H_{22}O_5$, M=354.5, crystallizes as low-diffracting pale-yellow needles; crystal dimensions 0.4×0.05× 0.02 mm, monoclinic, a=9.031(6), b=11.549(9), c=17.533(9) Å, β=100.20(3)°, V=1800(2) Å^3, space group P $2_1/a$, μ(Cu Kα)=0.76 mm^{-1}, Z=4, d_{calc}=1.31 Mg m^{-3}, final conventional R=0.092 and R_w=0.094 for 841 reflections with $F\geq4\sigma(F)$. Goodness of fit=2.26.

4.2.3. Crystal structure of 1c. Crystal data: $C_{42}H_{44}O_{10}\cdot CHCl_3$, M=828.2, crystallizes as transparent colourless prisms; crystal dimensions 1.0×0.2×0.1 mm, triclinic, a=12.009(5), b=20.815(3), c=8.529(2) Å, α=98.11(2), β=101.39(3), γ=97.78(3)°, V=2039(1) Å^3, space group P-1, μ(Cu Kα)=2.52 mm^{-1}, Z=2, d_{calc}=1.35 Mg m^{-3}, final conventional R=0.062 and R_w=0.077 for 3730 reflections with $F\geq6\sigma(F)$. Goodness of fit=2.09.

4.2.4. Crystal structure of 2a. Crystal data: $C_{76}H_{72}O_{16}$, M=1241.4, crystallizes as colourless platelets; crystal dimensions 0.5×0.4×0.1 mm, monoclinic, a=23.026(9), b=11.42(1), c=23.497(7) Å, β=96.98(3)°, V=6132(8) Å^3, space group $P2_1/n$, μ(Cu Kα)=0.77 mm^{-1}, Z=4, d_{calc}=1.35 Mg m^{-3}, final conventional R=0.064 and R_w=0.079 for 1600 reflections with $F\geq6\sigma(F)$. Goodnes of fit=1.74.

4.3. Materials

p-Toluenesulphonyl chloride (98%), diethyleneglycol (99%), triethyleneglycol (99%) and tetrathyleneglycol (99%) were purchased from Aldrich and have been used without further purification. Dry K_2CO_3 was obtained by overnight heating of analytical grade K_2CO_3 (Carlo Erba) at 110°C. Dry DMF was purchased from Fluka. Spectroscopy grade chloroform (Carlo Erba) was used in the kinetic experiments without further purification. The triethylene glycol bis-(*p*-toluenesulfonate) **3b** was prepared according to literature.[28] The preparation of 1,7-bis-(4-formylphenyl)-1,4,7-trioxaheptane **4a** and 1,7-bis-(4-[*trans* 3-(4-hydroxyphenyl)-3-oxo-propenyl]-phenyl)-1,4,7-trioxaheptane **5a**, was already described.[1]

4.3.1. 1,10-Bis-(4-formylphenyl)-1,4,7,10-tetraoxadecane (4b). A solution containing **3b** (16.19 g, 35.3 mmol) in dry DMF (50 mL) was added dropwise (ca. 1 h) to a stirred suspension in dry DMF (50 mL) of 4-hydroxybenzaldehyde (9.40 g, 77 mmol) and dry K_2CO_3 (26 g, 188 mmol), kept under argon at 80°C. The stirring was continued at this temperature for 3.5 h. The resulting mixture was filtered to remove K_2CO_3 and the solvent removed in vacuo to yield a solid residue. The recovered K_2CO_3 was dissolved in water and repeatedly extracted with CH_2Cl_2 to remove traces of bis-aldehyde. The dichloromethane extracts and the solid residue were combined, washed with aqueous NaOH (5%) until complete removal of unreacted 4-hydroxybenzaldehyde, water (3×40 mL) and dried on Na_2SO_4. The solvent was removed in vacuo to yield a solid that was crystallized from MeOH affording **4b** (9.32 g, 29.6 mmol, 81%, mp 77–78°C); lit. (54%, 74–75°C).[29]

4.3.2. 1,10-Bis-(4-[*trans* 3-(4-hydroxyphenyl)-3-oxo-propenyl]-phenyl)-1,4,7,10-tetraoxadecane (5b). The bis-aldehyde **4b** (1.32 g, 3.69 mmol) and 4-hydroxyacetophenone (1.51 g, 11.1 mmol) were added to a stirred solution of NaOH (1.34 g, 33.5 mmol) in EtOH/H_2O (8:2, 25 mL), kept at ~0°C under argon atmosphere. After the addition, the suspension was stirred at 50°C for ~48 h until complete consumption of the bis-aldehyde **4b**, as established by reverse phase TLC (eluent: CH_3CN/H_2O 1:1 +0.1% TFA). The mixture was cooled, carefully acidified to pH 5.5 by HCl 6N and then iced water was added until complete separation of a yellow powdered solid, that was filtered and repeatedly washed with iced water. Recrystallization from EtOH/H_2O yielded the bis-(4-hydroxychalcone) **5b** as yellow solid (86%, mp 119–120°C).

^{1}H NMR (DMSO-d_6),§ δ=3.18 [bs, O*H*], 3.62 [s, 4H, –O–CH_2], 3.72–3.82 [m, 4H, –O–CH_2], 4.10–4.20 [m, 4H, –O–CH_2], 6.88 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 4H, *H*-3′], 6.99 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 4H, *H*-3″], 7.61 [d, $^3J_{H-H}$=15.6 Hz, 2H, *H*-1], 7.71 [d, $^3J_{H-H}$=15.6 Hz, 2H, *H*-2], 7.76 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 4H, *H*-2′], 8.02 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 4H, *H*-2″].

^{13}C NMR (DMSO-d_6),§ δ=67.33, 68.88, 69.95 [–O–*C*H_2], 114.85 [*C*-3″], 115.32 [*C*-3′], 119.61 [*C*-2], 127.57 [*C*-quat.], 129.30 [*C*-2″], 130.54 [*C*-2′], 131.03 [*C*-quat.], 142.65 [*C*-1], 160.34 [*C*-quat.], 162.04 [*C*-quat.], 187.04 [*C*=O].

IR ($CHCl_3$), $\nu_{max(C=O)}$ 1673 cm^{-1}.

MS (IS) *m*/*z*=595 (M+H)$^+$.

Anal. calcd for $C_{36}H_{34}O_8$ C 72.71, H 5.76. Found C 72.92, H 5.62.

4.3.3. General procedure for the preparation of 9,12,15,18,30,33,36,39-octaoxapentacyclo-[38.2.2.2^{5,8}.2^{19,22}.2^{26,29}]-pentaconta-1(42),3,5,7,19,21,23,26,28,40,43,45,47,49-tetradecaene-2,25-dione (1b) and 9,12,15,27,30,33,36,39-octaoxapentacyclo-[38.2.2.2^{5,8}.2^{16,19}.2^{23,26}]-pentaconta-1(42),3,5,7,16,18,20,23,25,40,43,45,47,49-tetradecaene-2,22-dione (1c). A solution containing **3b** (or **3c**) (1 mmol) in dry DMF (200 mL) was added dropwise (ca. 5 h), to a stirred suspension of **5b** (or **5a**) (1 mmol) and dry K_2CO_3 (690 mg, 1 mmol) in dry DMF (800 mL) and kept under argon at 80°C. The stirring was continued at this temperature for ~3 days until complete consumption of **5**, as established by reverse phase TLC (CH_3CN/H_2O 7:3). The resulting mixture was cooled and filtered to remove K_2CO_3. The recovered K_2CO_3 was washed with DMF, the organic phases were collected and solvent removed in vacuo to yield a solid residue that was dissolved in $CHCl_3$, washed with water and dried on Na_2SO_4. The solvent was removed in vacuo to yield a solid that was purified by flash chromatography ($CHCl_3$/acetone 9:1). Recrystallization from $CHCl_3$/MeOH yielded the cyclic bis-chalcone **1b** (55%, mp 203–204°C) or **1c** (51%, mp 161–162°C) as yellow solid.

Compound **1b**. ^{1}H NMR ($CDCl_3$),§ δ=3.72 and 3.76 [partially superimposed singlets, 8H, –O–CH_2], 3.80–3.90 [m, 8H, –O–CH_2], 4.05–4.15 [m, 8H, –O–CH_2], 6.86 [AA′XX′, $^3J_{H-H}$=8.6 Hz, 4H, *H*-3″], 6.89 [AA′XX′, $^3J_{H-H}$=8.9 Hz, 4H, *H*-3′], 7.32 [d, $^3J_{H-H}$=15.5 Hz, 2H, *H*-2], 7.48 [AA′XX′, $^3J_{H-H}$=8.6 Hz, 4H, *H*-2′], 7.70 [d, $^3J_{H-H}$=15.5 Hz, 2H, *H*-1], 7.92 [AA′XX′, $^3J_{H-H}$=8.9 Hz, 4H, *H*-2′].

^{13}C NMR ($CDCl_3$),‡,§ δ=67.46, 67.49, 69.54, 69.63, 70.94, 70.97 [–O–*C*H_2], 114.35 [*C*-3′], 115.02 [*C*-3″], 119.30 [*C*-2], 127.80 [*C*-quat.], 130.03 [*C*-2″], 130.58 [*C*-2′], 131.31 [*C*-quat.], 143.65 [*C*-1], 160.70 [*C*-quat.], 162.45 [*C*-quat.], 188.43 [*C*=O].

UV–vis ($CHCl_3$), λ_{max} 336 nm, ε 5.0×10^4 cm^{-1} dm^3 mol^{-1}.

IR ($CHCl_3$), $\nu_{max(C=O)}$ 1656 cm^{-1}.

MS (IS) *m*/*z*=709 (M+H)$^+$.

Anal. calcd for $C_{42}H_{44}O_{10}$ C 71.17, H 6.26. Found C 71.40, H 6.16.

Compound **1c**. ^{1}H NMR ($CDCl_3$),§ δ=3.65–3.80 [m, 8H, –O–CH_2], 3.85–4.00 [m, 8H, –O–CH_2], 4.06–4.13 [m, 4H, –O–CH_2], 4.13–4.20 [m, 4H, –O–CH_2], 6.80 [AA′XX′, $^3J_{H-H}$=8.7 Hz, 4H, *H*-3″], 6.88 [AA′XX′, $^3J_{H-H}$=8.7 Hz, 4H, *H*-3′], 7,33 [d, $^3J_{H-H}$=15.5 Hz, 2H, *H*-2], 7.46 [AA′XX′, $^3J_{H-H}$=8.7 Hz, 4H, *H*-2″], 7.73 [d, $^3J_{H-H}$=15.5 Hz, 2H, *H*-1], 7.92 [AA′XX′, $^3J_{H-H}$=8.7 Hz, 4H, *H*-2′].

^{13}C NMR ($CDCl_3$),‡,§ δ=67.64, 67.70, 69.44, 69.96, 70.81 [–O–*C*H_2], 114.28 [*C*-3′], 115.36 [*C*-3″], 119.11 [*C*-2], 127.80 [*C*-quat.], 129.88 [*C*-2″], 130.53 [*C*-2′], 131.25 [*C*-quat.], 143.66 [*C*-1], 160.66 [*C*-quat.], 162.43 [*C*-quat.], 188.28 [*C*=O].

UV–vis ($CHCl_3$), λ_{max} 336 nm, ε 3.9×10^4 cm^{-1} dm^3 mol^{-1}.

IR ($CHCl_3$), $\nu_{max(C=O)}$ 1655 cm^{-1}.

MS (IS) *m*/*z*=709 (M+H)$^+$.

Anal. calcd for $C_{42}H_{44}O_{10}$ C 71.17, H 6.26. Found C 71.42, H 6.18.

4.3.4. General procedure for the preparation of 9,12,15,18,30,33,36,39-octaoxaheptacyclo-[38.2.2.2^{5,8}.2^{19,22}.2^{26,29}.0^{2,25}.0^{3,24}]-pentaconta-1(42),5,7,19,21,26,28,40,43,45,47,49-dodecaene-4,23-dione (2b) and 9,12,15,27,30,33,36,39-octaoxaheptacyclo-[38.2.2.2^{5,8}.2^{16,19}.2^{23,26}.0^{2,22}.0^{3,21}]-pentaconta-1(42),5,7,16,18,20,23,25,40,43,45,47,49-dodecaene-4,20-dione (2c). *Photoisomerization in sunlight*. A solution of **1b** or **1c** (0.163 mmol) in 50 mL of chloroform, kept in a Pyrex flask, was exposed to sunlight on a sunny day of April. The progress of the reaction was followed by silica gel TLC ($CHCl_3$) and reverse phase TLC (CH_3CN/H_2O 8:2). The reaction was stopped after ~2 h. The solution was evaporated and the residue purified by flash chromatography (**2b**: $CHCl_3$/acetone 8:2, 68%; **2c**: $CHCl_3$/acetone 9:1, 71%). Recrystallization from chloroform-methanol (**2b**) or acetone (**2c**) gave microscopic white needles of an analytically pure sample. (**2b**: mp 183–184°C; **2c**: mp 203–204°C).

Photoisomerization at 350 nm. A 6.44×10^{-3} mol dm^{-3} solution of **1b** or **1c** (25 mL) in chloroform, contained in a Pyrex flask, was irradiated in a Rayonet reactor by 14 lamps whose emission was centred at 350 nm. After ca. 30 min the reaction appeared to be completed. The solvent was removed and the residue purified by flash chromatography (yield: **2b**, 81%; **2c**, 86%).

§ For the sake of simplicity, the atom numbers indicated in NMR spectra are referred to those indicated in Scheme 2 (compounds **1b**, **1c** and **5b**), and Figure 5 (compound **2c**; N.B., in the case of **2b**: 2″a=2″d=2″, 3″b=3″c=3″).

‡ Erratum: in Ref. 1 is reported an erroneous assignment for C-3′ and C-3″ of **1a**. The correct assignment is: 114.64 [*C*-3′], 115.34 [*C*-3″].

Compound **2b**. ^{1}H NMR (acetone-d_6, 45°C),§ δ=3.52 [s, 4H, –O–CH_2], 3.60–3.65 [m, 4H, –O–CH_2] and partially superimposed 3.69 [s, 4H, –O–CH_2], 3.75–3.85 [m, 4H, –O–CH_2], 4.05–4.25 [m, 8H, –O–CH_2], 4.57 [m, 2H, *H*-1],¶ 5.19 [m, 2H, *H*-2],¶ 6.67 and 6.70 [two partially superimposed AA′XX′ systems, $^3J_{H-H}$=8.8 Hz, 6H, *H*-3′ and *H*-3″], 7.03 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 2H, *H*-2″], 7.74 [AA′XX′, $^3J_{H-H}$=8.8 Hz, 4H, *H*-2′].

^{13}C NMR (acetone-d_6, 45°C),§ δ=43.39 [*C*-1], 47.19 [*C*-2)], 68.93, 69.04, 70.13, 71.77, 72.08 [–O–*C*H_2], 114.66 [*C*-3′], 115.66 [*C*-3″], 130.06 [*C*-2″], 131.12 [*C*-quat.], 131.38 [*C*-2′], 133.33 [*C*-quat.], 157.85 [*C*-quat.], 163.43 [*C*-quat.], 197.75 [*C*=O].

UV–vis (CHCl$_3$), λ_{max} 273 nm, ε 2.8×10^4 cm^{-1} dm^3 mol^{-1}.

IR (CHCl$_3$), $\nu_{max(C=O)}$ 1677 cm^{-1}.

MS (IS) *m*/*z*=709 (M+H)$^+$.

Anal. calcd for $C_{42}H_{44}O_{10}$ C 71.17, H 6.26. Found C 71.44, H 6.14.

Compound **2c**. ^{1}H NMR (acetone-d_6, 45°C),§ δ=3.52–3.59 [m, 4H, –O–CH_2], 3.62 [ps, 8H, –O–CH_2], 3.78–3.85 [m, 4H, –O–CH_2], 4.07–4.14 [m, 4H, –O–CH_2], 4.16–4.22 [m, 4H, –O–CH_2], 4.52 [m, 2H, *H*-1],¶5.21 [m, 2H, *H*-2],¶ 6.55 [dd, $^3J_{H-H}$=8.4 Hz, $^4J_{H-H}$=2.5 Hz, 2H, *H*-3″c], 6.63 [dd, $^3J_{H-H}$=8.5 Hz, $^4J_{H-H}$=2.5 Hz, 2H, *H*-3″b], 6.70 [dd, $^3J_{H-H}$=8.3 Hz, $^4J_{H-H}$=2.2 Hz, *H*-2″d] and partially superimposed 6.74 [AA′XX′, $^3J_{H-H}$=9.0 Hz, *H*-3′], 7.18 [dd, $^3J_{H-H}$=8.5 Hz, $^4J_{H-H}$=2.3 Hz, 2H, *H*-2″a], 7.77 [AA′XX′, $^3J_{H-H}$=9.0 Hz, 4H, *H*-2′].

^{13}C NMR (acetone-d_6, 45°C),§ δ=44.32 [*C*-1], 45.95 [*C*-2], 68.90, 69.49, 70.14, 70.83, 71.39, 71.54 [–O–*C*H$_2$], 114.78 [*C*-3′], 116.47 [*C*-3″b], 116.78 [*C*-3″c], 128.41 [*C*-2″a], 131.18 [*C*-quat.], 131.36 [*C*-2′], 131.97 [*C*-2″d], 133.35 [*C*-quat.], 157.98 [*C*-quat.], 163.59 [*C*-quat.], 197.80 [*C*=O].

UV–vis (CHCl$_3$), λ_{max} 274 nm, ε 3.2×10^4 cm^{-1} dm^3 mol^{-1}.

IR (CHCl$_3$), $\nu_{max(C=O)}$ 1678 cm^{-1}.

MS (IS) *m*/*z*=709 (M+H)$^+$.

Anal. calcd for $C_{42}H_{44}O_{10}$ C 71.17, H 6.26. Found C 71.45, H 6.16.

The ^{1}H NMR and ^{13}C NMR spectra of **2a** in acetone-d_6 are reported here for comparison.

Compound **2a**. ^{1}H NMR (acetone-d_6, 45°C),§ δ=3.52–3.59 [m, 4H, –O–CH_2], 3.75–3.85 [m, 4H, –O–CH_2], 4.15–4.25 [m, 4H, –O–CH_2], 4.25–4.35 [m, 4H, –O–CH_2], 4.56 [m, 2H, *H*-1],¶5.22 [m, 2H, *H*-2],¶ 6.55 [dd, $^3J_{H-H}$=8.4 Hz, $^4J_{H-H}$=2.5 Hz, 2H, *H*-3″c], 6.62 [dd, $^3J_{H-H}$=8.5 Hz, $^4J_{H-H}$=2.5 Hz, 2H, *H*-3″b], 6.69 [AA′XX′, $^3J_{H-H}$=9.0 Hz, *H*-3′] and partially superimposed 6.71 [dd, $^3J_{H-H}$=8.5 Hz, $^4J_{H-H}$=2.5 Hz, *H*-2″d], 7.17 [dd, $^3J_{H-H}$=8.5 Hz, $^4J_{H-H}$=2.3 Hz, 2H, *H*-2″a], 7.67 [AA′XX′, $^3J_{H-H}$=9.0 Hz, 4H, *H*-2′].

^{13}C NMR (acetone-d_6),§ δ=43.66 [*C*-1], 46.22 [*C*-2], 69.02, 69.52, 70.63, 70.81 [–O–*C*H_2], 115.23 [*C*-3′], 116.49 [*C*-3″b], 116.81 [*C*-3″c], 128.51 [*C*-2″a], 131.32 [*C*-quat.], 131.42 [*C*-2′], 132.03 [*C*-2″d], 133.49 [*C*-quat.], 157.94 [*C*-quat.], 163.47 [*C*-quat.], 197.89 [*C*=O].

4.4. Kinetic measurements

A chloroform solution (0.3–1×10^{-5} mol dm^{-3}) of **1a**, **1b** or **1c**, kept in a quartz cell, was immersed in a pyrex vessel filled with water maintained at 25°C, and irradiated at regular time intervals by an arrangement of six 419 nm centred lamps, in a Rayonet reactor. The progress of the reaction was followed by recording the UV–vis spectrum. The spectra showed the presence of a isosbestic point (**1a**, 290 nm; **1b**, 292 nm; **1c**, 293 nm) and the regular decrease of the absorbance of the chalcone and the increase of the absorbance of the cyclobutane, according to a first order process.

¶ The estimated *J* values for this AA′BB′ scheme are reported in Table 1.

References

1. Cibin, F. R.; Doddi, G.; Mencarelli, P. *Tetrahedron* **2003**, *59*, 3455–3459.
2. Stobbe, H.; Bremer, K. *J. Prakt. Chem.* **1929**, *123*, 1–60.
3. Mustafa, A. *Chem. Rev.* **1952**, *51*, 1–23.
4. Wynberg, H.; Groen, M. B.; Kellogg, R. M. *J. Org. Chem.* **1970**, *35*, 2828–2830.
5. Schmidt, G. M. J. *Pure Appl. Chem.* **1971**, *27*, 647–678.
6. Montaudo, G.; Caccamese, S. *J. Org. Chem.* **1973**, *38*, 710–716.
7. Egerton, P. L.; Hyde, E. M.; Trigg, J.; Payne, A.; Beynon, P.; Mijovic, M. V.; Reiser, A. *J. Am. Chem. Soc.* **1981**, *103*, 3859–3863.
8. Toda, F.; Tanaka, K.; Kato, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1315–1318.
9. D'Auria, M. *Heterocycles* **2001**, *54*, 475–496.
10. Lewis, F. D.; Quillen, S. L.; Hale, P. D.; Oxman, J. D. *J. Am. Chem. Soc.* **1988**, *110*, 1261–1267.
11. Akabori, S.; Kumagai, T.; Habata, Y.; Sato, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2459–2466.
12. Akabori, S.; Kumagai, T.; Habata, Y.; Sato, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1497–1505.
13. Akabori, S.; Habata, Y.; Nakazawa, M.; Yamada, Y.; Shindo, Y.; Sugimura, T.; Sato, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3453–3455.
14. Zitt, H.; Dix, I.; Hopf, H.; Jones, P. G. *Eur. J. Org. Chem.* **2002**, 2298–2307.
15. Shoppee, C. W.; Wang, Y.-S.; Sternhell, S.; Brophy, G. C. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1880–1886.
16. D'Auria, M.; Emanuele, L.; Esposito, V.; Racioppi, R. *ARKIVOC* **2002**, *XI*, 65–77, http://www.arkat-usa.org/ark/journal/2002/Spinelli/MS-575H/575H.pdf
17. Nakanishi, H.; Hasegawa, M.; Mori, T. *Acta Crystallogr., Sect. C: Crystallogr. Struct. Commun.* **1985**, *C41*, 70–71.
18. Rabinovich, D. *J. Chem. Soc. (B)* **1970**, 11–16.
19. Gawronski, J. Conformations, Chiroptical and Related Spectral Properties of Enones. In *The Chemistry of Enones*;

Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; pp 81–85.
20. Schweizer, B. Structural Chemistry of Enones. In *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; pp 35–36.
21. At variance with **2a**, the NOESY studies of **2c** have been carried out in acetone-d_6/$CDCl_3$ solutions (2.5:1, 45°C), rather than in pure $CDCl_3$, because in this solvent **2c** seems to form aggregates, as suggested by the presence in the ^1H NMR spectra of a downfield shift of the signal of water and of broad signals for all the protons, that result in spin diffusion in the NOESY spectra (in pure acetone-d_6 the solubility of **2c** is too low for reliable 2D NMR experiments).
22. Montaudo, G.; Caccamese, S.; Librando, V. *Org. Magn. Reson.* **1974**, *6*, 534–536.
23. Caccamese, S.; McMillan, J. A.; Montaudo, G. *J. Org. Chem.* **1978**, *43*, 2703–2704.
24. The coupling constants were calculated by simulation of the AA′BB′ system by MestRe-C 2.3 program, Departamento de Química Orgánica, Universidade de Santiago de Compostela-1706 Santiago de Compostela, SPAIN: http://www.mestrec.com/
25. At this wavelength the absorbances of the chalcones **1a**–**1c** are almost negligible and the reactions are sufficiently slow to be followed by the used procedure. For irradiation at 350 nm the substrates are completely transformed into products in less than 5 s.
26. Burla, M. C.; Camalli, M.; Carrozzini, B.; Cascarano, G. L.; Giacovazzo, C.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **2003**, *36*, 1103.
27. Sheldrick, G. M., *SHELXTL*; Siemens: Madison, WI, 1996; Vol. 5.
28. Ouchi, M.; Kanzaki, T.; Inoue, Y.; Hakushi, T. *J. Org. Chem.* **1984**, *49*, 1408–1412.
29. Katritzky, A. R.; Belyakov, S. A.; Denisko, O. V.; Maran, U.; Dalal, N. S. *J. Chem. Soc., Perkin Trans. 2* **1998**, 611–615.