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Tetrahedron
Tetrahedron 63 (2007) 586–593

2-Hydroxy-1,2,2-triphenylethanone as an efficient photolabile protecting group for carboxylic acids

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Received 14 September 2006; revised 18 October 2006; accepted 2 November 2006
Available online 27 November 2006

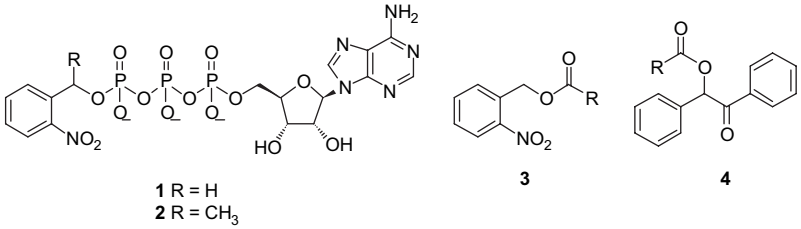
Abstract—The synthesis is reported of 2-hydroxy-1,2,2-triphenylethanone esters of carboxylic acids by the reaction between 2-chloro-1,2,2-triphenylethanone and a carboxylic acid in the presence of silver carbonate and silver tetrafluoroborate. Photolysis of the esters occurs rapidly on irradiation with a medium-pressure mercury lamp through quartz or Pyrex to return the carboxylic acid. The side product of the photolysis is benzo[*b*]phenanthro[9,10-*d*]furan, formed through a tandem process involving initial generation of 2,3-diphenylbenzofuran, photochemical cyclisation and re-aromatisation by aerial oxidation.

1. Introduction

The last two decades have seen a resurgence in interest in photolabile protecting groups. First reported in the 1960s, the use of photolabile protecting groups was slow to catch on until pioneering work by Kaplan et al. demonstrated that 2-nitrobenzyl ATP **1** (Scheme 1) and the α-methylated derivative **2**—so called 'caged' ATP—could be used as photoreactive triggers for biochemical processes, thereby opening up a very productive area of research in the photoliberation of biomolecules.[1]

Time-resolved biological experiments may be performed in which the phototrigger synchronises the production of short-lived intermediates, the build-up of which may be followed by fast X-ray diffraction,[2] infrared spectroscopy,[3] voltage clamp, patch clamp or other physiological recording techniques.[4] Other important applications of the technology include the preparation of spatially addressable arrays of macromolecules,[5–7] microlithography,[8] the synthesis of complex organic molecules,[9] and the controllable addition of reagents in analytical chemistry.[10] In the field of protein chemistry, some very exciting developments have been reported, including photoprotection of active-site residues,[11] the preparation of proteins containing unnatural photoprotected residues[12] and the use of a phototrigger to study protein folding.[13]

Carboxylic acids are one of the most common functional groups to be 'caged' by photolabile protecting groups, and recently a number of new protecting groups have been introduced, including *p*-hydroxyphenacyl,[14] ketoprofenate,[15] 7-*N*,*N*-diethylaminocoumarin,[16] 3-nitro-2-naphthalenemethanol,[17] α-keto amides,[18] 1-acyl-7-nitroindolines,[19] 2-(dimethylamino)-5-nitrophenyl[20] and α-carboxy nitrobenzyl.[21] Nevertheless, the two most widely used photolabile derivatives of carboxylic acids are esters of 2-nitrobenzyl alcohol **3** and benzoin **4**. The nitrobenzyl 'cage'[22] suffers



Scheme 1.

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doi:10.1016/j.tet.2006.11.015

from relatively slow kinetics for acid release, but more importantly, the side products of the photolysis are electrophilic nitroso aldehydes and ketones, which can alkylate nucleophilic protein residues, causing modifications leading to inhibition.[23] Further reaction of the nitroso side products leads to the production of diazo compounds, which are very efficient light screens, leading to a reduction in the efficiency of deprotection as the photolysis proceeds. Benzoin esters, first reported by Sheehan and Wilson, photolyse smoothly and rapidly with high quantum yield to give the acid and an inert benzofuran as the side product.[24] However, one drawback to their application as photolabile protecting groups for chiral biomolecules is that benzoin itself possesses a stereogenic centre, leading to an undesirable mixture of diastereoisomers of the protected target and the associated complications in purification and characterisation.

We envisaged that an achiral molecule closely related to benzoin, 2-hydroxy-1,2,2-triphenylethanone **5**, might also function as a photolabile protecting group for carboxylic acids,[25] and indeed carbamates derived from **5** have been shown to liberate amines upon irradiation.[26] The mechanism for the latter photocleavage process is unknown and the side products have not been identified, but the available data suggest a complex process in which several competing pathways are in operation. Herein we report the synthesis and characterisation of the 2-oxo-1,1,2-triphenylethyl esters of a range of carboxylic acids, including biologically relevant targets, detailed photolysis studies and the characterisation of the photolytic side product.

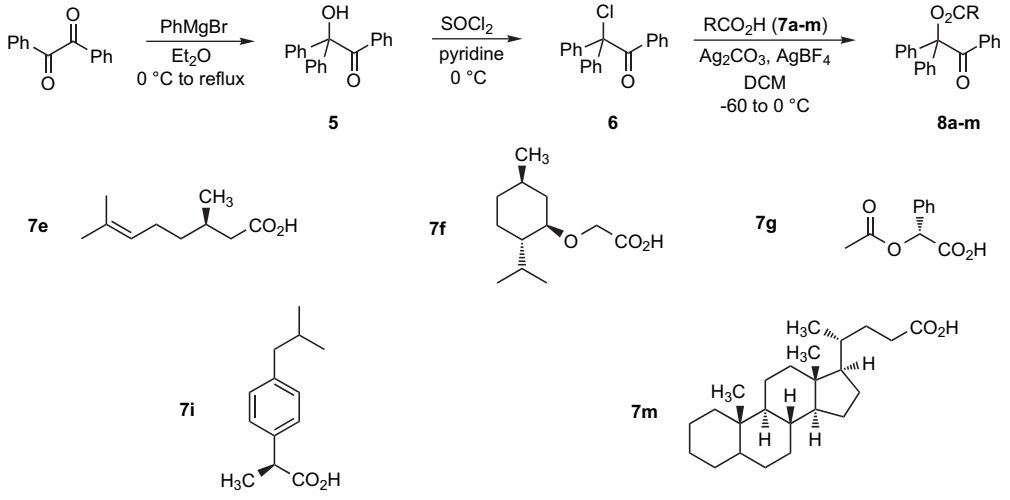
2. Results and discussion

The alcohol required to prepare our photolabile esters, 2-hydroxy-1,2,2-triphenylethanone **5**, was prepared by a Grignard reaction between phenyl magnesium bromide and benzil. As anticipated, esterification of this very hindered alcohol required forcing conditions. Thus, direct acylation of **5** with acetic anhydride required the use of refluxing pyridine as solvent, giving the acetate **8a** in 70% yield after 4 days. Consequently, we sought a milder method, which would be applicable to a wide range of carboxylic acids. We have previously reported the synthesis of benzoin esters via the displacement of bromide anion from desyl bromide by a caesium carboxylate, suggesting that a similar process could provide a facile route to the desired esters.[27]

Conversion of the alcohol **5** into the chloride **6** occurred smoothly in 64% yield upon treatment with thionyl chloride in pyridine.[28] Direct S_N2 displacement of chloride from the hindered tertiary centre in **6** would be unfavourable, and so we sought conditions that would favour a more S_N1-like process. Ohwada and Shudo demonstrated that the chloride **6** could undergo silver-assisted ionisation in dichloromethane solution at −60 °C to afford around 50% of the corresponding cation.[29] In their experiments, addition of water trapped the cation to yield the alcohol **5** along with recovered chloride. We hoped that trapping of the cation by a carboxylic acid or a carboxylate anion could be used to synthesise the corresponding ester. Disappointingly, treatment of **6** in dichloromethane solution at −60 °C with 2 equiv of silver acetate returned unreacted starting material. However, addition of 2 equiv of silver tetrafluoroborate to the −60 °C solution resulted in a 92% yield of the acetate ester **8a** after only 30 min.

Since it is inconvenient to have to pre-form the silver carboxylate we examined whether acetic acid could be employed directly in the transformation. Treatment of chloride **6** with 2 equiv each of silver tetrafluoroborate and acetic acid resulted in sluggish formation of the acetate **8a** in a modest 37% yield. Addition of caesium carbonate (which we had successfully used in our earlier work)[27] suppressed the reaction completely, presumably due to the insolubility of the caesium carboxylate in the reaction solvent. Silver carbonate, on the other hand, gave a much improved 75% yield of ester **8a**, and warming the reaction to 0 °C increased the yield to 89% (Scheme 2).

These esterification conditions were found to be applicable to a range of carboxylic acids (Table 1). The optimised protocol, suitable for the more hindered acids, involved reaction at −60 °C for 1 h, followed by 1–2 h at 0 °C; isolated yields



Scheme 2.

Table 1

Acid		Ester	Yield of ester (%)	Recovery of acid following photolysis (%)
7a	Acetic	**8a**	89	88
7b	Propanoic	**8b**	73	86
7c	Hexanoic	**8c**	74	91
7d	Benzoic	**8d**	54	86
7e	(*R*)-(+)-Citronellic	**8e**	74	82
7f	(−)-Menthoxyacetic	**8f**	77	86
7g	(*R*)-(−)-*O*-Acetylmandelic	**8g**	74	89
7h	3-Methylbutanoic	**8h**	71	90
7i	(*S*)-(+)-4-Isobutyl-α-methylphenylacetic	**8i**	64	73
7j	*O*-Acetylsalicylic	**8j**	59	79
7k	Diphenylacetic	**8k**	68	81
7l	Adamantylacetic	**8l**	89	74
7m	Cholanic	**8m**	80	83

were typically in excess of 70%. The range of carboxylic acids studied encompassed aromatic as well as straight chain and branched aliphatic examples, and included a number of chiral substrates. In contrast with benzoin esters of chiral acids,[27] purification and NMR analysis of the 2-hydroxy-1,2,2-triphenylethanone esters were not complicated by the presence of diastereoisomers. Some of the acids studied are of biological importance, including the steroid cholanic acid **7m**, a bile acid, aspirin **7j** and (*S*)-(+)-4-isobutyl-α-methylphenylacetic acid, the non-steroidal anti-inflammatory agent ibuprofen **7i**.

Deprotection was effected by irradiating the esters using a 400 W medium-pressure mercury lamp in methanol or ethanol solution, or in a mixed solvent system of ethanol and acetonitrile, without precautions to exclude air. Photolysis was rapid and quantitative as judged by TLC and NMR, and recovered yields of carboxylic acid were all high (Table 1). In the case of the chiral esters **8e–g**, **8i** and **8m**, the stereochemical integrity of the carboxylic acid was not compromised by the protection–deprotection sequence, as judged by the optical rotation of the recovered acid. The successful 'caging' and release of molecules such as aspirin, ibuprofen and cholanic acid suggest that the esters show promise in biological experiments or drug release applications.

A time course for the release of benzoic acid from a 10 mM solution of **8d** was plotted by measuring the amount of free acid present at a series of time intervals using HPLC (Fig. 1). As can be seen, quantitative deprotection was achieved after around 2 h of irradiation using a 400 W medium-pressure mercury lamp.

The release of acetic acid from **8a** was followed by both NMR and FTIR spectroscopy (Figs. 2 and 3a–d). In the NMR experiment, a 50 mM solution of **8a** was irraditated through Pyrex using a 400 W medium-pressure mercury lamp, with periodic monitoring by ^{1}H NMR; *N*-carbobenzyloxyalanine was used as an internal standard to quantify the extent of photolysis.

In the FTIR experiments, a 100 mM solution of **8a** in EtOD/CH_3CN (1:1) was irradiated using a 400 W medium-pressure mercury lamp in a solution cell with CaF_2 windows. In Figure 3a, the progress of the photolysis can be followed by loss of the ester stretch at ca. 1750 cm^{-1} and appearance of acetic acid at ca. 1725 cm^{-1}; Figure 3b shows the same data in the form of difference spectra. By repeating the experiment with 2 equiv of triethylamine in the solution, the stretch due to acetic acid is replaced by the much lower frequency stretch due to acetate at around 1570 cm^{-1}, enabling the decay of the ketone stretch at ca. 1700 cm^{-1} to be followed (Fig. 3c and d).

Recovered yields of the side product from the photolysis were low, suggesting that further photolytic events were occurring leading to photodegradation. However, basic extraction to remove the liberated acid, followed by chromatography of the residue allowed the isolation and full characterisation of a pure sample of benzo[*b*]phenanthro[9,10-*d*]furan **9**, suggesting that the photolysis occurs by a benzoin-like pathway (Scheme 3).[30] We propose that initial benzoin-like photolysis of **8** produces 2,3-diphenylbenzofuran **10**, which undergoes photochemical cyclisation to **11**; aerial oxidation re-aromatises the system to yield **9**.

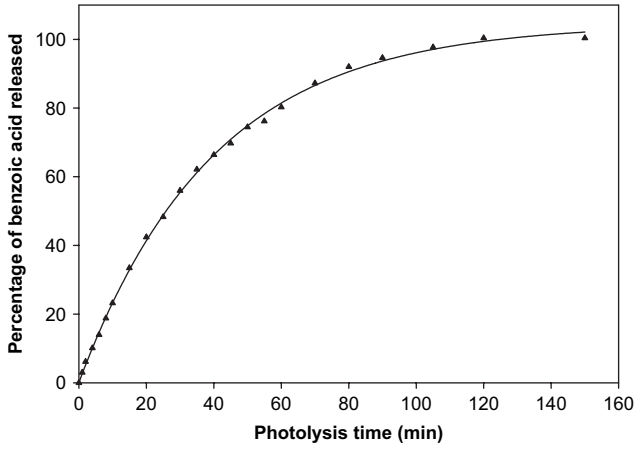


Figure 1. Release of benzoic acid monitored by HPLC. Irradiation of a 10 mM solution of **8d** in EtOH/CH_3CN (1:1) in a quartz tube was performed using a 400 W medium-pressure mercury lamp.

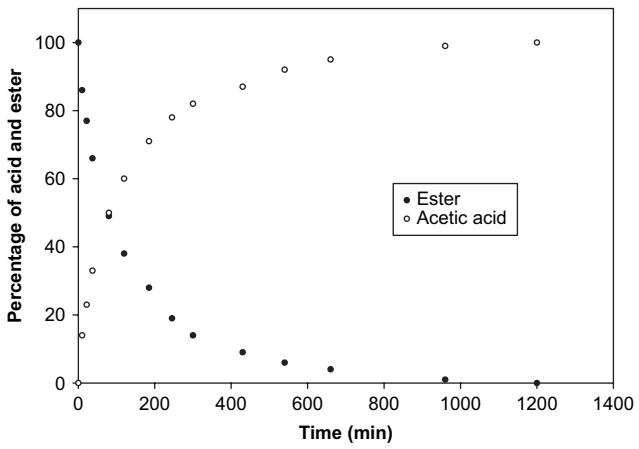


Figure 2. Release of acetic acid monitored by ^{1}H NMR. Irradiation of a 50 mM solution of **8a** in $CDCl_3$ was performed using a 400 W medium-pressure mercury lamp.

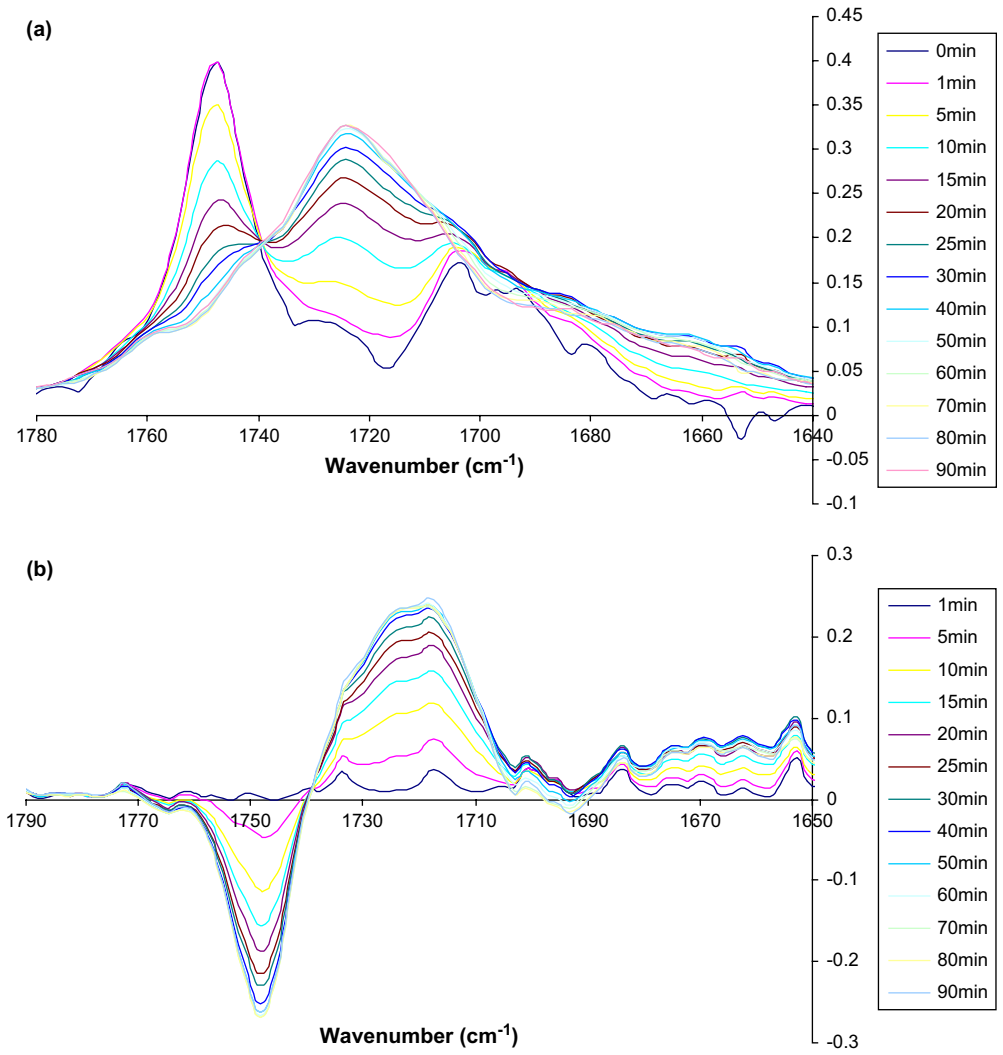


Figure 3. (a) Photolysis of a 100 mM solution of **8a** in EtOD/CH_3CN (1:1) using a 400 W medium-pressure mercury lamp, monitored by FTIR; (b) Representation of (a) in the form of difference spectra; (c) Photolysis of a 100 mM solution of **8a** in EtOD/CH_3CN (1:1) with the inclusion of 2 equiv of Et_3N, using a 400 W medium-pressure mercury lamp, monitored by FTIR; (d) Representation of (c) in the form of difference spectra.

Photochemical cyclisation of compounds related to **10** has previously been reported.[31]

This mechanism was further supported by UV monitoring experiments. Figure 4 shows the UV spectra of a sample of acetate **8a** in ethanol, recorded before and after irradiation for 1 and 18 min with a 16 W medium-pressure mercury lamp. The spectra appear to be consistent with the postulated tandem processes. Initial benzoin-like photolysis gives a rapid build-up of 2,3-diphenylbenzofuran **10**, evident by an increased absorption at around 300 nm in the spectrum recorded after 1 min.[32] Spectra recorded over the next 5 min (not shown) are complex, indicating the presence of at least two species. On prolonged irradiation, benzo[*b*]-phenanthro[9,10-*d*]furan **9** clearly emerges, and after 18 min **9** is the sole species evident in the UV spectrum.[33]

In conclusion, we have identified 2-hydroxy-1,2,2-triphenylethanone **5** as a new photolabile protecting group for carboxylic acids, which may be attached in good yield under mild reaction conditions. Photolytic deprotection to produce the carboxylic acid proceeds rapidly and in excellent yield, with the protecting group undergoing a novel tandem photocyclisation process to afford benzo[*b*]phenanthro[9,10-*d*]-furan **9**.

3. Experimental

3.1. General chemical procedures

Dichloromethane was distilled from calcium hydride.

^1H and ^{13}C NMR spectra were recorded on Bruker AC-300 or AV-300 spectrometer (300 and 75 MHz for ^1H and ^{13}C) or a Bruker AMX400 spectrometer (400 and 100 MHz for ^1H and ^{13}C), using deuterated solvent as the lock and were referenced downfield from tetramethylsilane. ^{13}C NMR spectra were recorded using the PENDANT pulse sequence. *J* values are reported in Hertz. The multiplicities of the spectroscopic signals are represented in the following manner; s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br s=broad singlet.

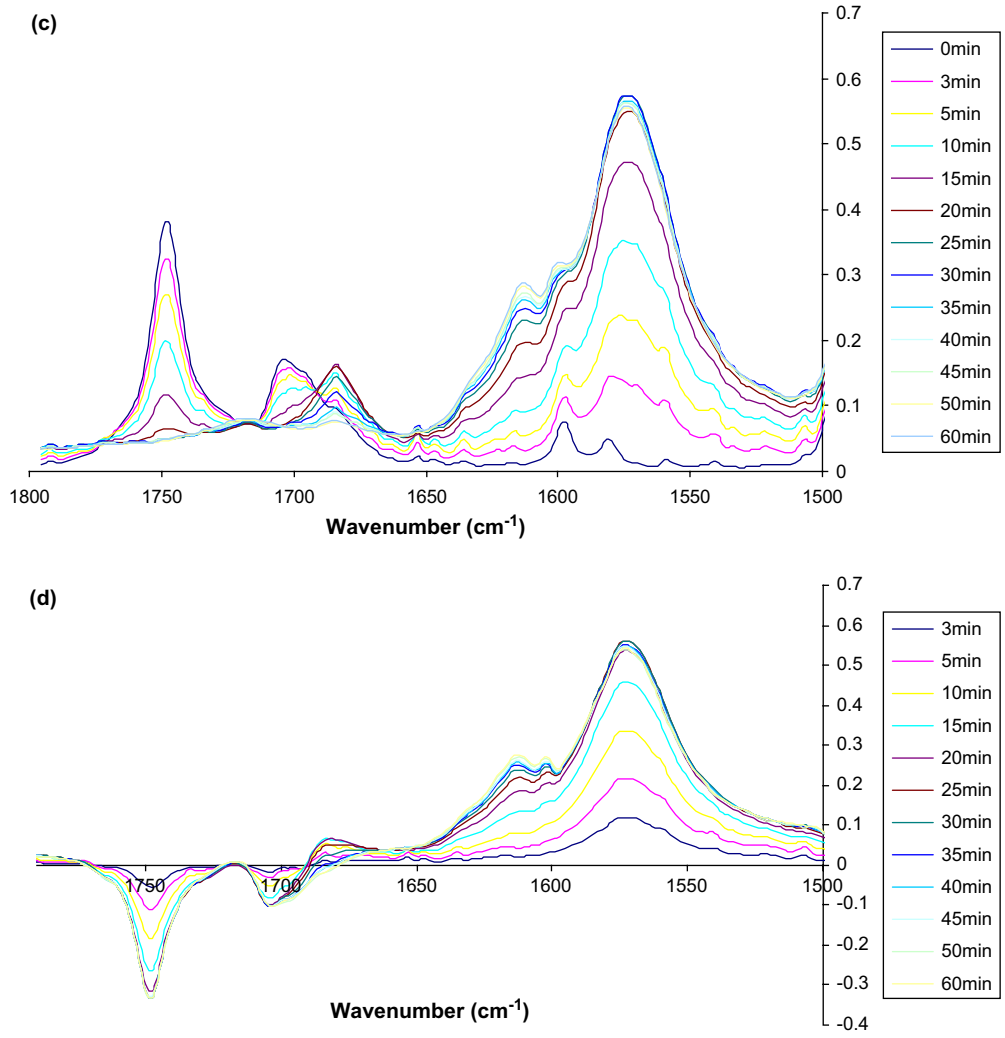


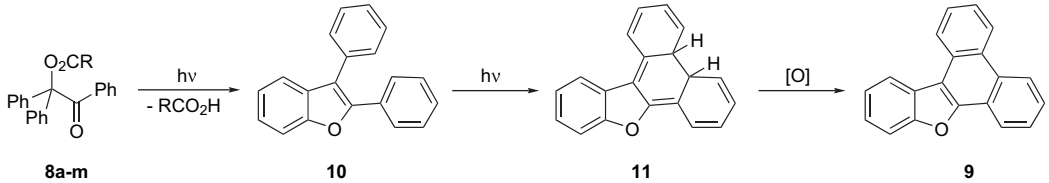
Figure 3. (*continued*)

Electron impact (EI) mass spectra were recorded on a VG Zabspec mass spectrometer. A Micromass LCT mass spectrometer was used for both low-resolution electrospray time of flight (ES-TOF) mass spectrometry (using a methanol mobile phase) and accurate mass measurement (using a lock mass incorporated into the mobile phase).

Thin layer chromatography was performed on precoated glass-backed silica gel plates supplied by ICN Ltd (Silica gel 60 F_{254}, thickness 0.25 mm). Column chromatography was performed on silica gel 40-63μ 60A (Fluorochem Ltd). HPLC was performed using a Dionex Summit HPLC system with Chromeleon software and a UVD170S UV–vis multi channel detector. Luna columns supplied by Phenomenex containing 10 μm C18 as the sorbent were used (column dimensions 250×4.6 mm).

3.2. Typical esterification procedure

To a solution of the acid (1.0 mmol) in anhydrous dichloromethane (15 mL) at −60 °C was added silver carbonate (1.0 mmol). The suspension was stirred for 20 min before 2-chloro-1,2,2-triphenylethanone **6** (0.5 mmol) was added, followed by silver tetrafluoroborate (1.0 mmol). After stirring at −60 °C for 1 h, the reaction mixture was removed to an ice bath for a further 1–2 h, until the reaction was judged to be complete by TLC. The reaction was quenched by the addition of water (10 mL) and then filtered through



Scheme 3.

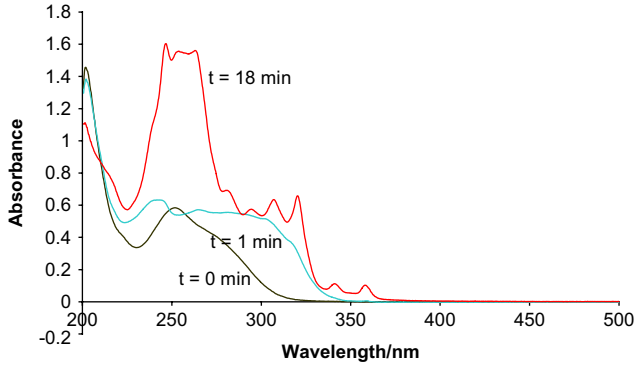


Figure 4.

a small pad of Celite to remove silver salts. The aqueous phase was extracted with dichloromethane (2×10 mL), the combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. Purification of the resulting esters was carried out by flash column chromatography.

3.3. Typical photolysis procedure

A solution of the ester (0.10 mmol) in EtOH/CH_3CN (1:1, 10 mL) was placed in a borosilicate glass tube and irradiated using a 400 W medium-pressure mercury lamp. On complete photolysis (as judged by TLC), the solvent was removed in vacuo and the residue was partitioned between dichloromethane (10 mL) and saturated sodium hydrogen carbonate solution (2×10 mL). The aqueous phase was acidified to pH 2 with 2 M HCl and extracted with dichloromethane (2×10 mL). The organic phase was dried ($MgSO_4$) and the solvent was removed in vacuo to yield the acid.

3.3.1. 2-Hydroxy-1,2,2-triphenylethanone 5. To a solution of benzil (15.80 g, 75.16 mmol) in anhydrous diethyl ether (200 mL) was added a 3 M solution of phenyl magnesium bromide (31.30 mL, 93.90 mmol) in diethyl ether dropwise over 1 h at 0 °C. After this time, the reaction mixture was heated under reflux for 4 h. Any remaining solid was removed by filtration and the filtrate was washed with 2 M hydrochloric acid (2×250 mL). The organic phase was dried ($MgSO_4$) and the solvent was removed in vacuo to yield a brown solid, which was recrystallised from petroleum ether to yield **5** as a colourless solid (7.19 g, 33%); mp 82–84 °C (lit.[29] 87–88 °C); ν_{max} (film)/cm^{-1} 1673 (C=O), 3027–3088 (aromatic CH) and 3438 (OH); δ_H ($CDCl_3$, 300 MHz) 4.99 (br s, 1H), 7.24–7.47 (m, 13H) and 7.72–7.75 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 85.19, 128.21, 128.23, 128.39, 128.46, 130.92, 133.02, 135.23, 142.02, 200.90; *m/z* (ES) 327 (100%, $[M+K]^+$) and 311 (28%, $[M+Na]^+$); Found (ES) $[M+Na]^+$, 311.1042. $C_{20}H_{16}O_2Na$ requires 311.1048. Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.24; H, 5.77%.

3.3.2. 2-Chloro-1,2,2-triphenylethanone 6. Dry pyridine (1.51 g, 1.55 mL, 19.2 mmol) was added to 2-hydroxy-1,2,2-triphenylethanone (5.00 g, 17.4 mmol) and warmed until a homogeneous solution formed. The solution was cooled in an ice bath until solid and then broken into small pieces. Thionyl chloride (2.62 g, 1.62 mL, 2.27 mmol) was added dropwise over 10 min with vigorous stirring and ice cooling and stirring was continued for a further hour at 0 °C. Ice cold water (100 mL) was added and the resulting mixture was extracted with diethyl ether (2×50 mL). The organic phase was dried ($MgSO_4$) and the solvent was removed in vacuo to yield a brown oil, which was recrystallised from petroleum ether to yield **6** as a colourless solid (3.41 g, 64%); mp 84–86 °C (lit.[29] 81.5–82 °C); ν_{max} (film)/cm^{-1} 1689 (C=O) and 3035–3089 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 7.32 (t, *J*=7.7, 2H), 7.40 (s, 10H), 7.47 (t, *J*=7.5, 1H), 7.89 (d, *J*=7.7, 2H); δ_C ($CDCl_3$, 75 MHz) 79.06, 127.87, 128.26, 128.56, 128.89, 131.15, 132.66, 134.66, 140.60, 195.58; *m/z* (ES) 271 (100%, $[(C_6H_5)_2CCOC_6H_5]^+$) and 329 (15%, $[M(^{35}Cl)+Na]^+$); Found (ES) $[M+Na]^+$, 329.0714. $C_{20}H_{15}ONaCl$ requires 329.0709. Anal. Calcd for $C_{20}H_{15}OCl$: C, 78.30; H, 4.93. Found: C, 78.52; H, 4.85%.

3.3.3. Acetic acid 2-oxo-1,1,2-triphenylethyl ester 8a. The general esterification procedure afforded **8a** as a colourless solid (147 mg, 89%); mp 148–151 °C (lit.[34] 147–148 °C); R_f=0.21 (petroleum ether/diethyl ether, 9:1); ν_{max} (film)/cm^{-1} 1698 (C=O), 1744 (ester C=O) and 2854–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 2.00 (s, 3H), 7.27–7.45 (m, 9H), 7.53–7.61 (m, 4H), 7.79–7.82 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 21.48, 89.04, 127.56, 128.07, 128.13, 128.33, 129.10, 132.04, 136.59, 139.77, 169.28, 195.28; *m/z* (ES) 353 (100%, $[M+Na]^+$); Found (ES) $[M+Na]^+$, 353.1148. $C_{22}H_{18}O_3Na$ requires 353.1154.

3.3.4. Propanoic acid 2-oxo-1,1,2-triphenylethyl ester 8b. The general esterification procedure afforded **8b** as a colourless solid (126 mg, 73%); R_f=0.33 (petroleum ether/diethyl ether, 9:1); mp 146–149 °C; ν_{max} (film)/cm^{-1} 1698 (C=O), 1744 (ester C=O) and 2859–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.93 (t, *J*=7.7, 3H), 2.29 (q, *J*=7.7, 2H), 7.24–7.41 (9H, m), 7.56–7.60 (m, 4H), 7.74–7.72 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 8.82, 28.20, 88.77, 127.57, 128.02, 128.03, 128.34, 129.14, 131.91, 136.78, 139.29, 172.44, 195.57; *m/z* (ES) 367 (92%, $[M+Na]^+$) and 271 (100%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 367.1315. $C_{23}H_{20}O_3Na$ requires 367.1310.

3.3.5. Hexanoic acid 2-oxo-1,1,2-triphenylethyl ester 8c. The general esterification procedure afforded **8c** as a colourless oil (140 mg, 74%); R_f=0.44 (petroleum ether/diethyl ether, 9:1); ν_{max} (neat)/cm^{-1} 1698 (C=O), 1744 (ester C=O) and 2854–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.73 (t, *J*=7.2, 3H), 0.90–1.00 (m, 2H), 1.09–1.20 (m, 2H), 1.34–1.44 (m, 2H), 2.26 (t, *J*=7.3, 2H), 7.27–7.43 (m, 9H), 7.56–7.60 (m, 4H), 7.74–7.78 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 13.90, 22.31, 24.15, 30.95, 34.56, 88.73, 127.62, 128.01, 128.31, 129.13, 131.86, 136.90, 139.93, 171.87, 195.65; *m/z* (ES) 409 (100%, $[M+Na]^+$) and 271 (98%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 409.1772. $C_{26}H_{26}O_3Na$ requires 409.1780.

3.3.6. Benzoic acid 2-oxo-1,1,2-triphenylethyl ester 8d. The general esterification procedure afforded **8d** as a colourless solid (104 mg, 54%); R_f=0.31 (petroleum ether/diethyl ether, 9:1); mp 128–132 °C (lit.[35] 145–146 °C); ν_{max} (film)/cm^{-1} 1698 (C=O), 1744 (ester C=O) and 2859–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 7.19 (t, *J*=7.55, 2H), 7.24–7.48 (m, 10H), 7.66 (d, *J*=7.35, 4H), 7.84 (d,

J=7.35, 2H), 8.04 (d, J=7.35, 2H); δ_C ($CDCl_3$, 75 MHz) 89.47, 127.54, 128.11, 128.45, 128.66, 129.19, 129.87, 132.02, 133.61, 136.42, 140.00, 164.84, 195.05; m/z (ES) 415 (100%, $[M+Na]^+$); Found (ES) $[M+Na]^+$, 415.1314. $C_{27}H_{20}O_3Na$ requires 415.1310. Anal. Calcd for $C_{27}H_{20}O_3$: C, 82.63; H, 5.14. Found: C, 82.66; H, 5.23%.

3.3.7. (*R*)-Citronellic acid 2-oxo-1,1,2-triphenylethyl ester 8e. The general esterification procedure afforded **8e** as a colourless oil (163 mg, 74%); R_f=0. 49 (petroleum ether/diethyl ether, 9:1); $[\alpha]_D^{17}$ +4 (c 0.2, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1698 (C═O), 1743 (ester C═O) and 2854–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.57 (d, J=6.6, 3H), 0.86–1.09 (m, 2H), 1.56 (s, 3H), 1.69 (s, 3H), 1.70–1.93 (m, 3H), 2.09 (dd, J=8.1, 15.4, 1H), 2.26 (dd, J=5.9, 15.4, 1H), 4.90–4.99 (m, 1H), 7.28–7.42 (m, 9H), 7.60–7.63 (m, 4H), 7.75–7.78 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 17.76, 19.22, 25.38, 25.81, 29.50, 36.44, 41.87, 88.76, 124.27, 127.68, 127.76, 128.03, 128.26, 128.29, 129.11, 131.45, 131.83, 136.96, 139.89, 139.93, 171.28, 195.70; m/z (ES) 463 (100%, [M+Na]$^+$); Found (ES) [M+Na]$^+$, 463.2265. $C_{30}H_{32}O_3Na$ requires 463.2249. Anal. Calcd for $C_{30}H_{32}O_3$: C, 81.79; H, 7.32. Found: C, 80.69; H, 7.33%.

3.3.8. Menthoxyacetic acid 2-oxo-1,1,2-triphenylethyl ester 8f. The general esterification procedure afforded **8f** as a colourless solid (182 mg, 77%); mp 130–133 °C; R_f=0.40 (petroleum ether/diethyl ether, 9:1); $[\alpha]_D^{17}$ −29 (c 0.2, $CHCl_3$); ν_{max} (film)/cm^{-1} 1698 (C═O), 1744 (ester C═O) and 2860–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.64 (d, J=7.0, 3H), 0.75–0.92 (m, 9H, including d, J=7.0, 6H), 1.08–1.23 (m, 2H), 1.54–1.63 (m, 2H), 1.66–1.76 (m, 1H), 2.11–2.23 (m, 1H), 2.74 (dt, J=4.2, 10.7, 1H), 4.01 (d, J=16.5, 1H), 4.08 (d, J=16.5, 1H), 7.23–7.45 (m, 9H), 7.54–7.61 (m, 4H), 7.76–7.79 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 16.27, 21.13, 22.35, 23.26, 25.44, 31.52, 34.44, 39.94, 48.22, 66.36, 80.47, 89.41, 127.64, 127.84, 128.09, 128.16, 128.22, 128.30, 128.41, 129.20, 132.04, 136.72, 139.53, 139.56, 169.16, 195.27; m/z (ES) 507 (100%, $[M+Na]^+$) and 271 (57%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 507.2517. $C_{32}H_{36}O_4Na$ requires 507.2511.

3.3.9. (*R*)-*O*-Acetylmandelic acid 2-oxo-1,2,2-triphenylethyl ester 8g. The general esterification procedure afforded **8g** as a colourless solid (168 mg, 74%); mp 116–117 °C; R_f=0.11 (petroleum ether/diethyl ether, 9:1); $[\alpha]_D^{17}$ −67 (c 0.2, $CHCl_3$); ν_{max} (film)/cm^{-1} 1698 (C═O), 1742 (ester C═O) and 2872–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 2.17 (s, 3H), 6.08 (s, 1H), 7.03 (t, J=7.7), 7.15 (d, J=7.35, 2H), 7.21–7.40 (m, 12H), 7.48–7.53 (m, 4H); δ_C ($CDCl_3$, 75 MHz) 20.66, 74.27, 90.53, 127.19, 127.71, 127.84, 127.93, 128.16, 128.17, 128.23, 128.36, 128.91, 129.03, 129.26, 131.86, 132.73, 135.81, 139.00, 139.12, 166.37, 169.74, 194.83; m/z (ES) 487 (100% $[M+Na]^+$) and 271 (10%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 487.1523. $C_{30}H_{24}O_5Na$ requires 487.1521. Anal. Calcd for $C_{30}H_{24}O_5$: C, 77.57; H, 5.21. Found: C, 77.36; H, 5.23%.

3.3.10. 3-Methylbutanoic acid 2-oxo-1,1,2-triphenylethyl ester 8h. The general esterification procedure afforded **8h** as a colourless oil (130 mg, 71%); R_f=0.48 (petroleum ether/diethyl ether, 9:1); ν_{max} (neat)/cm^{-1} 1698 (C═O), 1744 (ester C═O) and 2871–3061 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.67 (d, J=6.6, 6H), 1.85–1.98 (m, 1H), 2.15 (d, J=7.3, 2H), 7.29–7.41 (m, 9H), 7.60–7.63 (m, 4H), 7.77–7.79 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 22.13, 25.17, 43.45, 88.71, 127.67, 128.02, 128.26, 129.10, 131.82, 136.93, 139.90, 171.15, 195.68; m/z (ES) 395 (63%, $[M+Na]^+$) and 271 (100%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 395.1622. $C_{25}H_{24}O_3Na$ requires 395.1623.

3.3.11. (*S*)-4-Isobutyl-α-methylphenylacetic acid 2-oxo-1,2,2-triphenylethyl ester 8i. The general esterification procedure afforded **8i** as a colourless oil (159 mg, 64%); R_f=0.40 (petroleum ether/diethyl ether, 9:1); $[\alpha]_D^{23}$ +17 (c 0.2, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1698 (C═O), 1740 (ester C═O) and 2868–3059 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.84–0.89 (m, 1H), 0.94 (d, J=6.6, 6H), 1.26 (d, J=7.35, 3H), 1.80–1.96 (m, 1H), 2.49 (d, J=7.35, 2H), 3.66 (q, J=7.35, 1H), 6.99 (d, J=7.9, 2H), 7.06 (d, J=7.9, 2H), 7.15–7.43 (m, 11H), 7.45–7.51 (m, 2H), 7.63 (d, J=7.7, 2H); δ_C ($CDCl_3$, 75 MHz) 17.52, 22.50, 30.39, 45.16, 45.48, 88.74, 127.27, 127.38, 127.51, 127.84, 127.91, 127.96, 128.17, 128.29, 129.09, 129.43, 131.68, 136.30, 136.63, 139.72, 139.93, 140.79, 172.17, 195.62; m/z (ES) 499 (100%, $[M+Na]^+$); Found (ES) $[M+Na]^+$, 499.2236. $C_{33}H_{32}O_3Na$ requires 499.2249.

3.3.12. *O*-Acetylsalicylic acid 2-oxo-1,2,2-triphenylethyl ester 8j. The general esterification procedure afforded **8j** as a colourless solid (130 mg, 59%); mp 124–126 °C; R_f=0.28 (petroleum ether/diethyl ether, 7:3); ν_{max} (film)/cm^{-1} 1698 (C═O), 1731 (ester C═O), 1771 (ester C═O) and 2868–3061 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 2.02 (s, 3H), 7.05 (d, J=8.1, 1H), 7.21–7.41 (m, 10H), 7.54 (dt, J=1.5, 7.7, 1H), 7.61 (d, J=7.35, 4H), 7.81 (d, J=7.35, 2H), 7.93 (dd, J=1.5, 7.9, 1H); δ_C ($CDCl_3$, 75 MHz) 20.82, 89.97, 123.58, 124.06, 126.09, 127.58, 128.10, 128.16, 128.40, 129.14, 131.00, 132.09, 134.01, 136.35, 139.55, 150.58, 162.92, 169.26, 194.93; m/z (ES) 473 (98%, $[M+Na]^+$) and 271 (100%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 473.1378. $C_{29}H_{22}O_5Na$ requires 473.1365. Anal. Calcd for $C_{29}H_{22}O_5$: C, 77.32; H, 4.92. Found: C, 77.42; H, 4.97%.

3.3.13. Diphenylacetic acid 2-oxo-1,2,2-triphenylethyl ester 8k. The general esterification procedure afforded **8k** as a colourless solid (161 mg, 68%); R_f=0.31 (petroleum ether/diethyl ether, 9:1); mp 128–132 °C; ν_{max} (film)/cm^{-1} 1699 (C═O), 1743 (ester C═O) and 2890–3061 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 4.99 (s, 1H), 6.84 (d, J=6.6, 4H), 7.13–7.33 (m, 15H), 7.45–7.52 (m, 4H), 7.65 (d, J=7.7, 2H); δ_C ($CDCl_3$, 75 MHz) 57.22, 89.51, 127.31, 127.86, 128.03, 128.12, 128.24, 128.57, 128.82, 129.07, 131.73, 136.82, 137.62, 139.45, 170.16, 195.63; m/z (ES) 505 (100%, $[M+Na]^+$) and 271 (35%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 505.1770. $C_{34}H_{26}O_3Na$ requires 505.1780. Anal. Calcd for $C_{34}H_{26}O_3$: C, 84.62; H, 5.55. Found: C, 84.35; H, 5.60%.

3.3.14. Adamantylacetic acid 2-oxo-1,2,2-triphenylethyl ester 8l. The general esterification procedure afforded **8l** as a colourless solid (202 mg, 89%); R_f=0.49 (petroleum ether/diethyl ether, 9:1); mp 48–50 °C; ν_{max} (film)/cm^{-1} 1697 (C═O), 1736 (ester C═O) and 2848–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 1.27 (s, 3H), 1.28 (s, 3H), 1.40

(br s, 1H), 1.43 (br s, 2H), 1.54 (br s, 2H), 1.58 (br s, 1H), 1.77 (br s, 3H), 1.98 (s, 2H), 7.23–7.40 (m, 9H), 7.56–7.62 (m, 4H), 7.71–7.75 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 28.58, 33.23, 36.60, 42.06, 48.73, 88.89, 128.03, 128.12, 128.17, 128.24, 129.06, 131.67, 137.30, 139.86, 170.07, 195.86; *m/z* (ES) 487 (100%, $[M+Na]^+$) and 271 (15%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 487.2261. $C_{32}H_{32}O_3Na$ requires 487.2249.

3.3.15. Cholanic acid 2-oxo-1,2,2-triphenylethyl ester 8m. The general esterification procedure afforded **8m** as a colourless solid (123 mg, 80%); mp 59–62 °C; R_f=0.38 (petroleum ether/diethyl ether, 9:1); $[\alpha]_D^{21}$ +36 (*c* 0.2, $CHCl_3$); ν_{max} (film)/cm^{-1} 1700 (C=O), 1743 (ester C=O) and 2861–3060 (aromatic CH); δ_H ($CDCl_3$, 300 MHz) 0.53 (s, 3H), 0.75 (d, *J*=6.2, 3H), 0.81–1.40 (m, 23H), 1.45–1.57 (m, 2H), 1.60–1.92 (m, 6H), 2.12–2.34 (m, 2H), 7.24–7.42 (m, 9H), 7.53–7.60 (m, 4H), 7.74 (d, *J*=7.7, 2H); δ_C ($CDCl_3$, 75 MHz) 12.27, 18.22, 20.97, 21.51, 24.35, 24.43, 26.72, 27.20, 27.41, 27.67, 28.23, 30.46, 31.56, 35.15, 35.52, 36.03, 37.75, 40.41, 40.66, 42.88, 43.88, 56.08, 56.72, 88.75, 127.55, 127.75, 128.04, 128.30, 128.38, 129.15, 131.90, 136.84, 139.91, 139.98, 172.30, 195.64; *m/z* (ES) 653 (100%, $[M+Na]^+$) and 271 (63%, $[(C_6H_5)_2CCOC_6H_5]^+$); Found (ES) $[M+Na]^+$, 653.3949. $C_{44}H_{54}O_3Na$ requires 653.3971.

3.3.16. Benzo[*b*]phenanthro[9,10-*d*]furan 9. R_f=0.45 (hexane); mp 154–156 °C (lit.[36] 156 °C); λ_{max} (methanol, log ε) 247 (4.92), 255 (4.92), 282 (4.38), 307 (4.53) and 320 (4.32); δ_H ($CDCl_3$, 300 MHz) 7.48–7.56 (m, 2H), 7.68–7.83 (m, 5H), 8.39–8.44 (m, 1H), 8.53–8.57 (m, 1H), 8.64–8.69 (m, 1H), 8.77–8.84 (m, 2H); δ_C ($CDCl_3$, 100 MHz) 111.99, 114.38, 121.71, 121.76, 122.25, 123.38, 123.44, 123.78, 124.15, 125.11, 125.46, 125.62, 127.10, 127.17, 127.46, 128.21, 128.59, 130.60, 151.23, 155.88; *m/z* (EI) 268 (100%, M^+); Found (EI) M^+, 268.0881. $C_{20}H_{12}O$ requires 268.0888.

Acknowledgements

We are grateful to the BBSRC for funding (grant BB/C50446X/1).

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