Regioselective Free Radical Cyclization: a General Method for the Synthesis of the Spiro[4.4]nonane System of Fredericamycin A

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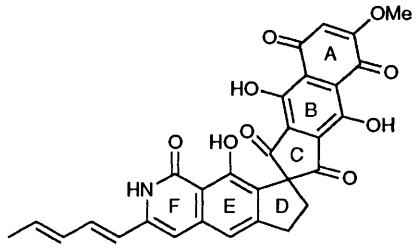
Introduction of a halogen atom at the middle carbon atom of cyclic 1,3-diketones is described. A convenient approach for constructing the spiro[4.4]nonane system of fredericamycin A has been demonstrated by halogen transfer during radical cyclization followed by reductive elimination of the halogen atom. The configuration of the bromo compound **6b** was confirmed by X-ray crystal structure analysis.

Fredericamycin A **1** is of especial interest in terms both of its potential antitumour activity and its complex structure, the latter containing a unique spiro[4.4]nonane system annulated on either side by naphthoquinone and isoquinoline entities which impart an L-shaped skeleton to the molecule.[1]



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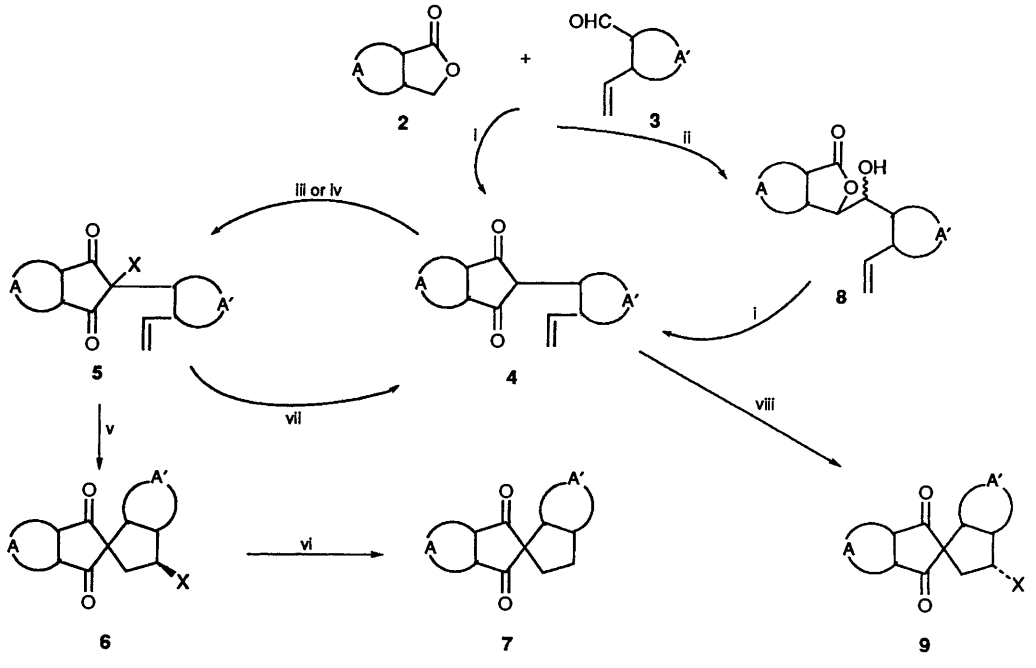
As part of the programme on the total synthesis of fredericamycin A, we have developed a strategy for the construction of the spiro[4.4]nonane system[2a] and, based on this methodology, have also reported the synthesis of the two main segments, the benzphthalide (ABC ring synthon)[3a,b] and the isoqinoline (DEF ring synthon).[4a,b] Also, we have recently reported a mild and general method for constructing the spiro system[2b] which, although working smoothly in several model systems,[2b] resulted in a very low yield when applied to the final construction of **1**. To overcome this, we have explored a new strategy that may be applied to the final synthesis of fredericamycin A.

Results and Discussion

Our new methodology involved the preparation of the 2-halogenoindanedione **5** by treating **4** with either $CuCl_2$ or $CuBr_2$ in acetic acid at room temperature for 2 h. Alternatively, **5** was made by Mn^{III} generation of free radicals followed by halogen addition either from $CuCl_2$ or preferably $CuBr_2$. Treatment of **5** with Ph_3SnH[6] (1 equiv.) and AIBN (0.03 equiv.) in benzene at 50 °C for 10 h led to efficient halogen transfer to give **6**. Further addition of $(Ph)_3SnH$ (1.1 equiv.) and refluxing of the mixture for 2 h gave reductive elimination of the halogen in **6** and formation of the spiro system **7** (see Scheme 1). This reaction is of a general nature, as evident by the various examples listed in Table 1. In all cases the halogen compound **6** gave only one isomer as evidenced by NMR



Scheme 1 *Reagents and conditions:* i, NaOMe, MeOH, ethylproprionate, reflux, 2 h; ii, LDA, THF, HMPA, −78 °C, 1.5 h; iii, $CuCl_2$ or $CuBr_2$, acetic acid, 1–2 h, room temp; iv, $CuCl_2$ or $CuBr_2$, manganese(III) acetate, acetic acid, 15 min, room temp; v, Ph_3SnH (1 equiv.), AIBN (0.03 equiv.), benzene, 10 h, 50 °C, slow addition; vi, Ph_3SnH (1.1 equiv.), reflux, 2 h; vii, Ph_3SnH (2 equiv.), AIBN (0.03 equiv.), benzene, reflux, 4 h; viii, HCl (gas) cat. amount, $CHCl_3$, 36 h, room temp.

spectroscopic evidence. The proton at the halogen-bearing carbon invariably appears as a triplet at δ 5.9, whose stereochemistry is not clear. Hence, we resorted to X-ray crystallography analysis of the parent spiro[4.4]nonane system **6b**. In all essential details, the geometry of the molecules, in terms of bond lengths and angles, showed normal values [the bromine atom is displaced 1.22 Å from the mean plane defined by atoms C(3')···C(9') and C(2)]. The bromine atom is symmetrical with respect to the two oxygen atoms (Br···O av. 5.25 Å) whilst the bromo substituted five-membered ring adopts a near-envelope conformation with the apex at C(1'), which is 0.4 Å out of the mean plane passing through the other four atoms. The two aromatic rings are twisted nearly at right angles as in the case of fredericamycin A.

Treatment of **4** with catalytic quantities of HCl gas in chloroform at room temperature for 36 h gave the spiro halogenated product **9**, in which the chlorine atom is α-orientated (proton at halogen-bearing carbon appear as dd δ 5.9). Compound **9** was not reduced by $(Ph)_3SnH$ and AIBN in refluxing benzene for 2 h.

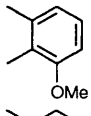
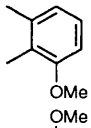
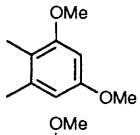
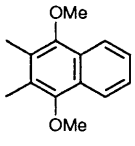
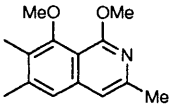
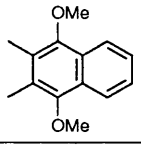
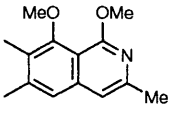
The above approach has been extended to the synthesis of fredericamycin A **1**.

Experimental

General Details.—M.p.s were recorded on Fisher-Johns melting point apparatus and are uncorrected. NMR spectra were obtained with a Varian Gemini (200 MHz) instrument. Tetramethylsilane was used as an internal reference and deuteriochloroform as solvent. *J* Values are given in Hz. IR spectra were recorded on a Shimadzu IR-470 spectrometer. Mass spectra were obtained by EI at 70 eV with Finnigan mat 1020B instrument. UV spectra were recorded in MeOH on a Shimadzu UV-160 spectrometer. Flash chromatography was performed on Merck silica gel (200 mesh) and the solvents ethyl acetate and light petroleum (b.p. 40–60 °C) were redistilled before use. All reactions were monitored by TLC on Merck silica gel $60F_{254}$ precoated glass plate (layer thickness 0.25 mm) and were visualised with UV light and then with phosphomolybdic acid solution. Organic extracts were dried over anhydrous Na_2SO_4 and solvents were removed on a Buchi rotary evaporator. Routinely, dry organic solvents were stored under nitrogen. Organic solvents were dried by distillation from the following: benzene and tetrahydrofuran (THF) (sodium benzophenone ketyl), dichloromethane ($LiAlH_4$) methanol (magnesium methoxide), ethyl proprionate ($CuSO_4$) and HMPA (CaH_2). Where necessary, reactions requiring anhydrous conditions were performed in a flame- or oven-dried apparatus under nitrogen.

General Preparation of Compound **4**.—To a suspension of the phthalide **2** (1 mmol) and the aldehyde **3** (1 mmol) in dry methanol (4 cm^3), ethyl proprionate (3 mmol) and sodium methoxide (3 mmol)[7] were added sequentially and the mixture refluxed for 3 h under nitrogen; it was then cooled to room temperature and the low-boiling materials were evaporated under reduced pressure. The resulting dark orange residue was dissolved in water, acidified with dil. HCl (up to pH 2) and extracted with dichloromethane. The combined extracts were washed with water and brine, dried (Na_2SO_4) and concentrated

Table 1

Entry	A	A'	X	Yield (%)* 5	6	7
a			Cl	86	60	55
b			Br	95	90	91
c			Cl	82	80	69
d			Br	85	81	82
e			Br	89	Not isolated	84
f			Br	83	Not isolated	97
g			Br	83	Not isolated	77
h			Br	79	Not isolated	74

* Yields of isolated products.

under reduced pressure to give a residue which was purified by column chromatography (silica gel, light petroleum–ethyl acetate, 9:1) to afford the dione **4**.

Compound **4a** *or* **4b**. M.p. 93–94 °C; ν_{max}(KBr)/cm^{-1} 1740, 1700, 1580, 1260, 1220 and 760; δ_H(200 MHz; $CDCl_3$) 8.06–8.16 (2 H, m), 7.80–7.89 (2 H, m), 7.48 (1 H, d, *J* 7.32), 7.18–7.36 (2 H, m), 6.92 (1 H, s), 6.84 (1 H, dd, *J* 18.32, 11.70), 5.62 (1 H, dd, *J* 18.32, 1.4), 5.29 (1 H, d, *J* 11.70) and 4.56 (1 H, s); λ_{max}(MeOH)/nm 322.6 and 251.6; *m*/*z* (EI) 248 (M^+), 233, 133, 116 and 104.

Compound **4c** *or* **4d**. M.p. 97–98 °C; ν_{max}($CHCl_3$)cm^{-1} 1740, 1700, 1590, 1490, 1290 and 780; δ_H(200 MHz; $CDCl_3$) 7.81 (1 H, t, *J* 7.66), 7.52 (1 H, d, *J* 7.26), 7.32 (1 H, d, *J* 7.26), 7.15–7.27 (4 H, m), 6.90 (1 H, dd, *J* 17.74, 11.07), 5.62 (1 H, dd, *J* 17.74, 1.4), 5.29 (1 H, dd, *J* 11.07, 1.4), 4.53 (1 H, s) and 4.02 (3 H, s); λ_{max}(MeOH)/nm 289.6, 248.4 and 238.6; *m*/*z* (EI) 278 (M^+), 263, 250, 235 and 191.

Compound **4e**. M.p. 134–135 °C; ν_{max}($CHCl_3$)/cm^{-1} 1740, 1700, 1585, 1260, 1230 and 760; δ_H(200 MHz; $CDCl_3$) 7.53 (1 H, d, *J* 9.12), 7.30 (1 H, d, *J* 7.54), 7.22 (1 H, m), 7.17 (1 H, d, *J* 7.5), 7.03 (1 H, d, *J* 1.88), 6.91 (1 H, dd, *J* 17.22, 10.95), 6.79 (1 H, d, *J* 1.88), 5.65 (1 H, dd, *J* 17.22, 1.4), 5.32 (1 H, dd, *J* 10.95, 1.4), 4.59 (1 H, s), 3.99 (3 H, s) and 3.95 (3 H, s); *m*/*z* (EI) 308 (M^+) and 193.

Compound **4f**. *Viscous material*; ν_{max}($CHCl_3$)/cm^{-1} 1745, 1700, 1580, 1255, 1225 and 750; δ_H(200 MHz; $CDCl_3$) 4.22 (6 H, s), 4.72 (1 H, s), 5.27 (1 H, dd, *J* 11.07, 1.4), 5.55 (1 H, dd, *J* 17.59, 1.4), 7.20 (1 H, dd, *J* 17.59, 11.07), 7.52 (1 H, d, *J* 8.87), 7.75–7.87 (3 H, m), 8.21 (1 H, d, *J* 8.87) and 8.45–8.54 (3 H, m); *m*/*z* (EI) 358 (M^+).

Compound **4g**. M.p. 67–68 °C; ν_{max}($CHCl_3$)cm^{-1} 1750, 1700 and 1690; δ_H(200 MHz; $CDCl_3$) 8.09–8.16 (2 H, m), 7.91–7.99 (2 H, m), 7.55 (1 H, s), 7.15 (1 H, dd, *J* 17.7, 11.1), 7.05 (1 H, s), 5.85 (1 H, dd, *J* 17.7, 1.4), 5.59 (1 H, dd, *J* 11.1, 1.4), 4.66 (1 H, s), 4.07 (3 H, s), 3.40 (3 H, s) and 2.53 (3 H, s); λ_{max}(MeOH)/nm 338 and 248; *m*/*z* (EI) 373 (M^+), 358, 342, 240 and 228.

Compound **4h**. *Viscous material*; ν_{max}(neat)/cm^{-1} 1735, 1701, 1610 and 760; δ_H(200 MHz; $CDCl_3$) 8.01–8.15 (2 H, m), 7.62 (1 H, s), 7.56 (1 H, s), 7.38–7.49 (2 H, m), 6.97 (1 H, dd, *J* 17.7, 11.0), 5.77 (1 H, dd, *J* 17.7, 1.4), 5.23 (1 H, dd, *J* 11.0, 1.4), 4.19 (1 H, s), 4.07 (6 H, s), 4.04 (3 H, s), 3.67 (3 H, s) and 2.48 (3 H, s); λ_{max}(MeOH)/nm 732, 658, 613, 581, 316 and 241; *m*/*z* (EI) 483 (M^+), 452, 421 and 225.

General Preparation of the Aldol Adduct **8**.—To the freshly prepared lithium diisopropylamide (generated from diisopropylamine (0.386 mmol) and BuLi (0.386 mmol) in THF (5 cm^3) at −78 °C were added the phthalide **2** (0.368 mmol) in THF (5 cm^3) and HMPA (3 mm^3, 0.368 mmol) and the mixture stirred for 15 min. The aldehyde **3** (0.368 mmol) in THF (2 cm^3) was added to the mixture which was then stirred for 1.5 h at −78 °C and for 5 min at room temperature. After being quenched with saturated ammonium chloride in aqueous ammonium hydroxide at −78 °C, the reaction mixture was extracted with ethyl acetate and the organic layer was washed with water, dried (Na_2SO_4) and concentrated. The residue obtained was purified by chromatography (silica gel, light petroleum–acetone–triethylamine 90.0:9.98:0.02) to give the aldol adduct **8**.

Compound **8e**. *Viscous material*; ν_{max}($CHCl_3$)/cm^{-1} 3410, 1755, 1580 and 760; δ_H(200 MHz; $CDCl_3$) 7.49–7.57 (3 H, m), 7.31–7.39 (3 H, m), 7.05 (1 H, dd, *J* 17.22, 10.99), 6.39 (1 H, d, *J* 1.69), 5.75 (1 H, dd, *J* 17.22, 1.2), 5.53–5.60 (2 H, m), 5.45 (1 H, dd, *J* 10.99, 1.2), 3.95 (3 H, s) and 3.65 (3 H, s); *m*/*z* (EI) 326 (M^+) and 308.

Compound **8f**. *Viscous oil*; ν_{max}($CHCl_3$)/cm^{-1} 3415, 1750, 1575, 1230 and 750; δ_H(200 MHz; $CDCl_3$) 8.42 (1 H, d, *J* 8.79), 8.16 (1 H, d, *J* 8.34), 7.50–7.76 (4 H, m), 7.31 (2 H, m), 7.21 (1 H, dd, *J* 17.31, 10.99), 5.88 (1 H, d, *J* 6.40), 5.81 (1 H, d, *J* 1.79), 5.70 (1 H, dd, *J* 17.3, 1.3), 5.45 (1 H, dd, *J* 10.99, 1.30), 4.27 (3 H, s), 4.05 (3 H, s) and 2.35 (1 H, d, *J* 6.73); *m*/*z* (EI) 376 (M^+) and 358.

Compound **8g**. M.p. 93–94 °C; ν_{max}($CHCl_3$)/cm^{-1} 3410, 1750, 1575, 1235 and 760; δ_H(200 MHz; $CDCl_3$) 7.87 (2 H, t, *J* 6.76), 7.50–7.68 (2 H, m), 7.49 (1 H, s), 7.15 (1 H, dd, *J* 15.55, 9.52), 6.95 (1 H, s), 5.82 (1 H, d, *J* 9.28), 5.60 (1 H, dd, *J* 15.55, 1.4), 5.30 (1 H, dd, *J* 9.52, 1.4), 5.10 (1 H, t, *J* 6.76), 4.12 (3 H, s), 3.90 (3 H, s) and 2.50 (3 H, s); *m*/*z* (EI) 391 (M^+) and 258.

Compound **8h**. M.p. 85–86 °C; ν_{max}($CHCl_3$)/cm^{-1} 3400, 1760, 1580, 1240 and 750; δ_H(200 MHz; $CDCl_3$) 8.42 (1 H, d, *J* 8.0), 8.22, 8.18 (1 H, d, two sets, *J* 8.0), 7.80–7.58 (2 H, m), 7.50, 7.42 (1 H, s, two sets), 7.40 (1 H, dd, *J* 16.0, 10.0), 7.02, 7.0 (1 H, s, two sets), 6.38, 5.98 (1 H, d, two sets, *J* 8.0), 5.90–5.18 (4 H, m), 4.38, 4.24 (3 H, s, two sets), 4.18 (6 H, s), 4.10, 4.02 (3 H, s, two sets) and 2.58, 2.56 (3 H, s, two sets); *m*/*z* (EI) 501 (M^+), 256 and 245.

General Procedure for the Compound **5**.—To compound **4** (0.02 mmol) in acetic acid (0.4 cm^3), were added $Mn(OAc)_3$ (0.2 mmol) and $CuCl_2$ or $CuBr_2$ (0.3 mmol) sequentially and the mixture was stirred for 15 min at room temperature. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, eluting with $CHCl_3$ to afford compound **5**.

Compound **5a**. *Viscous oil*; ν_{max}($CHCl_3$)/cm^{-1} 1730, 1580, 1478, 1285 and 760; δ_H(200 MHz; $CDCl_3$) 8.10–8.15 (2 H, m), 7.91–8.01 (2 H, m), 7.28–7.47 (4 H, m), 6.42 (1 H, dd, *J* 17.5, 10.0), 5.3 (1 H, dd, *J* 17.5, 1.4) and 4.98 (1 H, dd, *J* 10.0, 1.4); *m*/*z* (EI) 282, 284 (M^+) and 247.

Compound **5b**. M.p. 98–99 °C; ν_{max}($CHCl_3$)/cm^{-1} 1735, 1578, 1480, 1280 and 750; δ_H(200 MHz; $CDCl_3$) 8.10–8.16 (2 H, m), 7.92–8.20 (2 H, m), 7.40–7.46 (2 H, m), 7.31–7.33 (2 H, m), 6.35 (1 H, dd, *J* 16.12, 10.99), 5.27 (1 H, dd, *J* 16.12, 1.4) and 4.95 (1 H, dd, *J* 10.99, 1.4); *m*/*z* (EI) 326, 328 (M^+), 247, 219, 191 and 104.

Compound **5c**. M.p. 122–123 °C; ν_{max}($CHCl_3$)/cm^{-1} 1740, 1585, 1480, 1278 and 758; δ_H(200 MHz; $CDCl_3$) 7.83–7.92 (2 H, m), 7.65 (1 H, d, *J* 7.65), 7.35–7.46 (4 H, m), 6.60 (1 H, dd, *J* 16.94, 10.91), 5.35 (1 H, dd, *J* 16.94, 1.4), 5.03 (1 H, dd, *J* 10.91, 1.4) and 4.10 (3 H, s); *m*/*z* (EI) 312 and 314 (M^+).

Compound **5d**. M.p. 134–135 °C; ν_{max}($CHCl_3$)/cm^{-1} 1745, 1590, 1480, 1290 and 760; δ_H(200 MHz; $CDCl_3$) 7.94 (1 H, dd, *J* 7.33, 7.33), 7.80 (1 H, d, *J* 7.33), 7.61 (1 H, d, *J* 7.33), 7.24–7.30 (4 H, m), 6.45 (1 H, dd, *J* 16.85, 10.67), 5.29 (1 H, dd, *J* 16.85, 1.4), 5.03 (1 H, dd, *J* 10.67, 1.4) and 4.06 (3 H, s); λ_{max}(MeOH)/nm 341, 242 and 224; *m*/*z* (EI) 356, 358 (M^+), 277, 263, 249 and 218.

Compound **5e**. *Viscous material*; ν_{max}($CHCl_3$)/cm^{-1} 1730, 1585, 1475, 1290 and 758; δ_H(200 MHz; $CDCl_3$) 7.86 (1 H, m), 7.32–7.40 (2 H, m), 7.34 (1 H, m), 7.08 (1 H, d, *J* 1.88), 6.82 (1 H, d, *J* 1.88), 6.62 (1 H, dd, *J* 17.7, 11.1), 5.35 (1 H, dd, *J* 17.7, 1.4), 5.08 (1 H, dd, *J* 11.1, 1.4), 4.03 (3 H, s) and 4.01 (3 H, s); *m*/*z* (EI) 387 (M^+), 307, 152 and 124.

Compound **5f**. *Viscous oil*; ν_{max}($CHCl_3$)/cm^{-1} 1735, 1592, 1482 and 1292; δ_H(200 MHz; $CDCl_3$) 8.47–8.53 (2 H, m), 7.78–7.86 (2 H, m), 7.32–7.47 (4 H, m), 6.45 (1 H, dd, *J* 15.55, 11.35), 5.4 (1 H, dd, *J* 15.55, 1.4), 5.01 (1 H, dd, *J* 11.35, 1.4) and 4.26 (6 H, s); *m*/*z* (EI) 436, 438 (M^+) and 358.

Compound **5g**. *Viscous material*; ν_{max}($CHCl_3$)/cm^{-1} 1730, 1700 and 1690; δ_H(200 MHz; $CDCl_3$) 8.10–8.18 (2 H, m), 7.90–7.93 (2 H, m), 7.52 (1 H, s), 7.10 (1 H, dd, *J* 17.7, 11.1), 6.92 (1 H, s), 5.73 (1 H, dd, *J* 17.7, 1.4), 5.42 (1 H, dd, *J* 11.1, 1.4), 4.03 (3 H, s), 3.45 (3 H, s) and 2.49 (3 H, s); λ_{max}(MeOH)/nm 337 and 248; *m*/*z* (EI) 452 (M^+), 437 and 372.

Compound **5h**. *Viscous oil*; ν_{max}($CHCl_3$)/cm^{-1} 1730, 1700 and 1688; δ_H(200 MHz; $CDCl_3$) 8.46–8.55 (2 H, m), 7.75–7.83 (2 H, m), 7.54 (1 H, s), 6.99 (1 H, s), 6.89 (1 H, dd, *J* 17.7, 11.3), 5.72 (1 H, dd, *J* 17.7, 1.4), 5.41 (1 H, dd, *J* 11.3, 1.4), 4.28 (6 H, s),

3.97 (3 H, s), 3.44 (3 H, s) and 2.51 (3 H, s); *m/z* (EI) 562 (M^+), 547, 500, 482 and 420.

General Procedure for Compound **6**.—A solution of AIBN (0.03 mmol) and Ph_3SnH (0.15 mmol) in benzene (12 cm^3) was added slowly over 10 h, through syringe pump at 50 °C, to compound **5** (0.15 mmol) in benzene (5 cm^3); the mixture was stirred at the same temperature for an additional 2 h. The mixture was evaporated and the residue purified by column chromatography (10% EtOAc–hexane eluent) to give compound **6**.

Compound **6a**. *Viscous material*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1745, 1705, 1465 and 855; δ_H(200 MHz; $CDCl_3$) 8.05–8.20 (2 H, m), 7.91–8.01 (2 H, m), 7.6 (1 H, d, *J* 7.41), 7.4 (1 H, t, *J* 7.32), 7.23 (1 H, t, *J* 7.32), 6.68 (1 H, d, *J* 7.41), 5.85 (1 H, t, *J* 7.33), 3.10 (1 H, dd, *J* 13.67, 7.33) and 2.86 (1 H, dd, *J* 13.67, 7.33); *m/z* (EI) 282, 284 (M^+) and 247.

Compound **6b**. M.p. 127–128 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1706, 1471 and 849; δ_H(200 MHz; $CDCl_3$) 8.04–8.18 (2 H, m), 7.94–8.20 (2 H, m), 7.58 (1 H, d, *J* 7.73), 7.40 (1 H, t, *J* 7.10), 7.18 (1 H, t, *J* 7.10), 6.65 (1 H, d, *J* 7.73), 5.90 (1 H, t, *J* 7.10), 3.15 (1 H, dd, *J* 14.0, 7.10) and 3.0 (1 H, dd, *J* 14.07, 7.10); *m/z* (EI) 326, 328 (M^+) and 247.

Compound **6c**. *Viscous oil*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1745, 1705, 1455 and 850; δ_H(200 MHz; $CDCl_3$) 7.88–7.97 (2 H, m), 7.56 (1 H, d, *J* 6.9), 7.01–7.38 (4 H, m), 5.89 (1 H, t, *J* 7.30), 4.10 (3 H, s), 3.12 (1 H, dd, *J* 13.63, 7.30) and 3.01 (1 H, dd, *J* 13.64, 7.30); *m/z* (EI) 312, 314 (M^+) and 277.

Compound **6d**. *Viscous material*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1708, 1450 and 845; δ_H(200 MHz; $CDCl_3$) 7.91–7.98 (2 H, m), 7.55 (1 H, d, *J* 6.70), 7.31–7.42 (4 H, m), 5.85 (1 H, t, *J* 7.20), 4.07 (3 H, s), 3.13 (1 H, dd, *J* 13.73, 7.20) and 2.98 (1 H, dd, *J* 13.73, 7.20); *m/z* (EI) 356, 358 (M^+) and 277.

General Procedure for Compound **7**.—To unpurified **6** was added Ph_3SnH (0.17 mmol) and the mixture was refluxed for 2 h at 80 °C. It was then concentrated and purified by column chromatography to afford compound **7**.

Compound **7a** *or* **7b**. *Syrup*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1714, 1700, 1510 and 990; δ_H(200 MHz; $CDCl_3$) 8.02–8.10 (2 H, m), 7.86–7.92 (2 H, m), 7.35 (1 H, d, *J* 8.06), 7.20 (1 H, d, *J* 6.67), 7.02 (1 H, t, *J* 7.90), 6.6 (1 H, d, *J* 7.49), 3.31 (2 H, t, *J* 6.4) and 2.45 (2 H, t, *J* 6.4); *m/z* (EI) 248 (M^+) and 133.

Compound **7c** *or* **7d**. *Viscous oil*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1720, 1700, 1520 and 1020; δ_H(200 MHz; $CDCl_3$) 7.82 (1 H, d, *J* 7.33), 7.80 (1 H, d, *J* 7.33), 7.63 (1 H, d, *J* 7.35), 7.15–7.30 (2 H, m), 7.01 (1 H, t, *J* 8.02), 6.7 (1 H, d, *J* 8.02), 4.04 (3 H, s), 3.28 (2 H, t, *J* 7.33), and 2.51–2.60 (2 H, m); λ_{max}(MeOH)/nm 330.4, 231.4 and 215; *m/z* (EI) 278 (M^+), 263, 250 and 219.

Compound **7e**. *Syrup*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1715, 1700, 1600, 1580 and 1050; δ_H(200 MHz; $CDCl_3$) 7.21–7.34 (2 H, m), 7.01–7.06 (2 H, m), 6.78 (1 H, d, *J* 1.92), 6.67 (1 H, d, *J* 7.5), 3.98 (3 H, s), 3.96 (3 H, s), 3.26 (2 H, t, *J* 7.47) and 2.6–2.65 (2 H, m); λ_{max}(MeOH)/nm 340, 240 and 210; *m/z* (EI) 308 (M^+) and 205.

Compound **7f**. *Viscous oil*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1715, 1700, 1350, 1020 and 750; δ_H(200 MHz; $CDCl_3$) 8.45–8.52 (2 H, m), 7.73–7.81 (2 H, m), 7.38 (1 H, d, *J* 8.65), 7.18 (1 H, d, *J* 8.08), 7.03 (1 H, t, *J* 7.45), 6.7 (1 H, d, *J* 7.51), 4.20 (6 H, s), 3.32 (2 H, t, *J* 7.47) and 2.63 (2 H, t, *J* 7.47); *m/z* (EI) 358 (M^+) and 328.

Compound **7g**. *Viscous material*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1700, 1579 and 1048; δ_H(200 MHz; $CDCl_3$) 8.07–8.15 (2 H, m), 7.79–7.87 (2 H, m), 7.38 (1 H, s), 7.01 (1 H, s), 4.1 (3 H, s), 3.5 (2 H, t, *J* 7.65), 3.34 (3 H, s), 2.66 (3 H, s) and 2.51–2.62 (2 H, m); λ_{max}(MeOH)/nm 227; *m/z* (EI) 373 (M^+) and 342.

Compound **7h**. *Viscous oil*; $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1700 and 760; δ_H(200 MHz; $CDCl_3$) 8.46–8.35 (2 H, m), 7.67–7.79 (2 H, m), 7.36 (1 H, s), 6.97 (1 H, s), 4.26 (6 H, s), 3.99 (3 H, s), 3.43 (3 H, s), 3.42 (2 H, t, *J* 7.5), 2.56 (2 H, t, *J* 7.5) and 2.47 (3 H, s); λ_{max}(MeOH)/nm 375, 337 and 276; *m/z* (EI) 483 (M^+), 453 and 438.

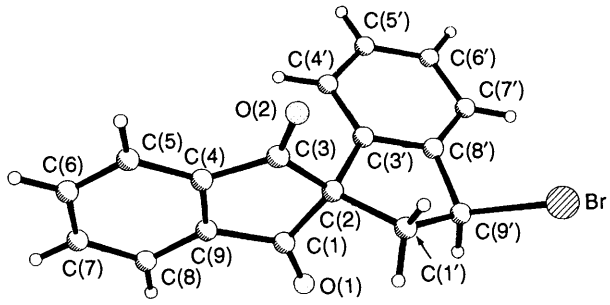


Fig. 1 X-Ray molecular structure for compound **6b**

Procedure for Compound **9a**.—To compound **4a** (0.2 mmol) in $CHCl_3$ (6 cm^3) was added HCl gas (catalytic amount) for 36 h at room temperature. The solvent was removed under reduced pressure and the residue chromatographed (10% EtOAc–hexane) to afford **9a** as a semi-solid (85%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1745, 1705, 1465 and 850; δ_H(200 MHz; $CDCl_3$) 8.12–8.20 (2 H, m), 7.88–7.98 (2 H, m), 7.60 (1 H, d, *J* 9.52), 7.17–7.40 (2 H, m), 6.67 (1 H, d, *J* 9.52), 5.92 (1 H, dd, *J* 7.05, 4.70), 2.85 (1 H, dd, *J* 14.11, 7.05) and 2.72 (1 H, dd, *J* 14.11, 4.70); *m/z* (EI) 282 and 284 (M^+).

Crystal Structure Analysis of Compound **6b**. *Crystal data*. $C_{17}H_{11}BrO_2$, *M* = 327.18, monoclinic, *a* = 10.328(2), *b* = 10.789(2), *c* = 12.529(3) Å, β = 96.74(2)°, *V* = 1386.4(5) $Å^3$, *Z* = 4, D_c = 1.567 mgm^{-3}, *F*(000) = 656. Space group $P2_1/n$. Mo-Kα radiation, λ = 710 69 Å, μ(Mo-Kα) = 29.31 cm^{-1}.

Pale yellow, needle-shaped crystals were obtained from ethyl acetate–hexane. A single crystal of dimension 0.15 × 0.10 × 0.19 mm was mounted on a Siemens R3M/V diffractometer and 25 reflections were used to determine accurate lattice parameters. Intensity data were collected in the range of $3 \leqslant 2\theta \leqslant 45°$ with graphite monochromotized Mo-Kα radiation by the ω–2θ scan technique at room temperature. Periodic measurement of standard reflections throughout data collection demonstrated their stability. The data were corrected for Lorentz and polarisation factors but no absorption corrections were made. Out of 2120 measured reflections 957 had $I \geqslant 3\sigma(I)$ and were considered observed.

Crystallographic calculations were performed by using the SHELXTL-plus [8] system of programs. The structure was solved by direct methods. The positions and anisotropic thermal parameters of non-hydrogen atoms were refined by full-matrix least-squares method. The hydrogen atoms were placed at calculated positions and allowed to ride on the parent carbon atom with fixed isotropic thermal parameters. Final values of *R* and R_w are 0.053 and 0.062, respectively. The weights were $\omega = 1/[\sigma^2(F_o) + 0.001\ F_o^2]$. The maximum highest values in the final difference map were 0.30 e $Å^{-3}$ and −0.21 e $Å^{-3}$. The scattering factors for neutral atoms and anomolous dispersion correction for bromine atom were those incorporated in SHELXTL-Plus. The geometrical parameters were calculated by using the program PARST.[9]

A perspective view with the crystallographic numbering scheme is shown in Fig. 1.*

* Final positional parameters, thermal parameters, fractional atomic coordinates of hydrogen atoms, bond lengths and bond angles and structure factor tables have been deposited at the Cambridge Crystallographic Data Centre (see section 5.6.3 of 'Instructions for Authors', January issue).

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