Synthesis of the Carbazole Alkaloids Hyellazole and 6-Chlorohyellazole and Related Derivatives

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We describe a new seven-stage synthesis of the carbazole alkaloids hyellazole and 6-chlorohyellazole, which proceeds *via* thermal cyclization of the 3-(buta-1,3-dienyl)indoles **7ab** and **7bb**, prepared from the condensation products of indole-2,3-diones **1a**, **b** and the 3-methyl-4-phenylbut-3-en-2-one **2b**. This procedure was also used to prepare related 3-methoxy-1-phenylcarbazole derivatives.

The synthesis of carbazole alkaloids has received considerable attention in the last few years.[1] This interest in the synthesis of alkaloids of the hyellazole–carbazomycin group is related to the fact that the carbazomycins are the first antibiotics to contain the carbazole nucleus.[2] We report a new synthesis of the 3-methoxycarbazole alkaloids hyellazole,[3] 6-chlorohyellazole[3] and of some related derivatives based on the strategy which involves thermal cyclization of 3-(buta-1,3-dienyl)indoles **7**.

This approach has found little use in the synthesis of carbazoles to date.[4] In our case, the presence of a good leaving group at the 2-position of the indole moiety of the 3-(buta-1,3-dienyl)indoles **7** eliminates the need for a dehydrogenation step and the loss of the methoxy group at the 3-position of the final products. Both hyellazole and 6-chlorohyellazole have been previously synthesized.[2,4,5]

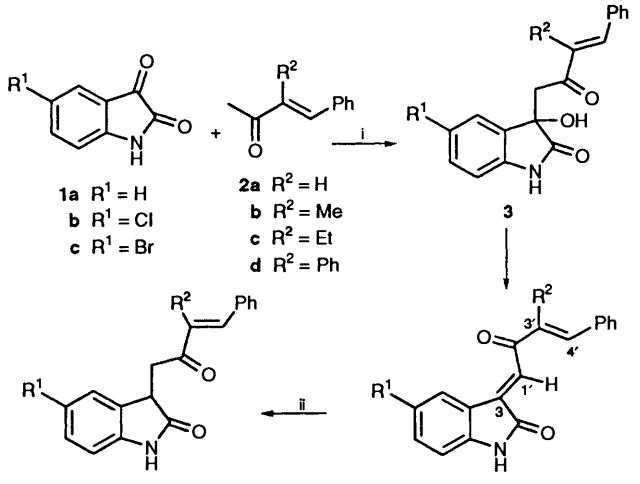
Results and Discussion

Our starting materials were the readily available indole-2,3-diones **1** and 4-phenylbut-3-en-2-ones **2**. The condensation of the indole-2,3-diones **1** with the 4-phenylbutenones **2** was carried out in EtOH and in the presence of diethylamine, as described for the reaction of indole-2,3-dione and acetophenone,[6] to give the corresponding 3-hydroxy derivatives **3**.

When the dehydration was performed with 36% HCl in EtOH (method A), the more usual method[6,7] for the dehydration of 3-hydroxy-3-(aroylmethyl)indol-2(3*H*)-ones, only in the case of compound **3aa** was the corresponding dehydrated derivative, in this case compound **4aa**, obtained. Compounds **4ab** and **4ac** were obtained by reaction with $SOCl_2$ in CH_2Cl_2 (method B) whereas the other derivatives (**4ad**, **4bb** and **4cc**) were prepared with Ph_3P–CCl_4 in tetrahydrofuran (THF) (method C). The reported *E* stereochemistry for the 3,1′ double bond in compounds **4** was assigned on the basis of literature data.[8] The stereochemistry of the 3′,4′ double bond was also assumed to be *E* from the ^1H coupling constant of the olefinic hydrogens (16.20–16.80 Hz) in compounds **3aa**, **4aa** and **5aa**.

The selective reduction of the 3,1′ double bond in compounds **4** to derivatives **5** was carried out as described for the 3-benzylideneindol-2(3*H*)-ones[6] with sodium hydrosulfite (Scheme 1). The results of all these reactions are reported in Table 1.

Attempted dehydration of compounds **3** (with the exception of **3aa**) with HCl–EtOH gave, in very good yield (Table 1), the



Scheme 1 *Reagents and conditions:* i, Et_2NH, EtOH, room temp.; ii, $Na_2S_2O_4$, aq. EtOH

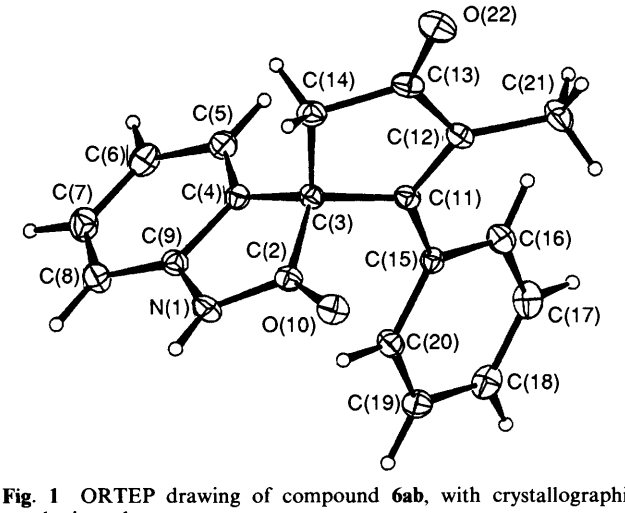


Fig. 1 ORTEP drawing of compound **6ab**, with crystallographic numbering scheme

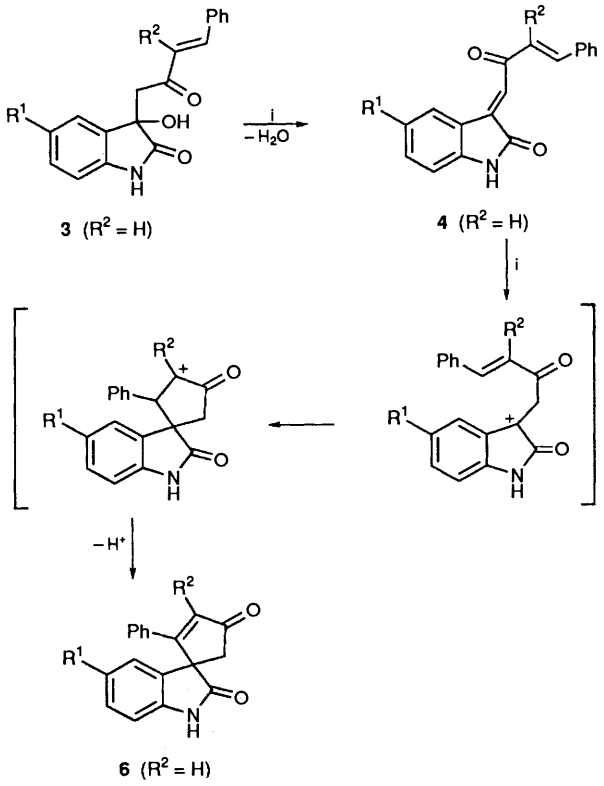
new derivatives **6**. The reported spirane structure for compounds **6** is based on analytical and spectroscopic data (Table 4, see later) as well as X-ray diffraction analysis† of compound **6ab**. Fig. 1 shows the molecular shape and the crystallographic numbering scheme whereas details of crystallographic data, data collection and structure refinement are reported in Table 5 (see later). Compounds **6** are formed from

† Crystallographic details have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge CB2 1EW, England.

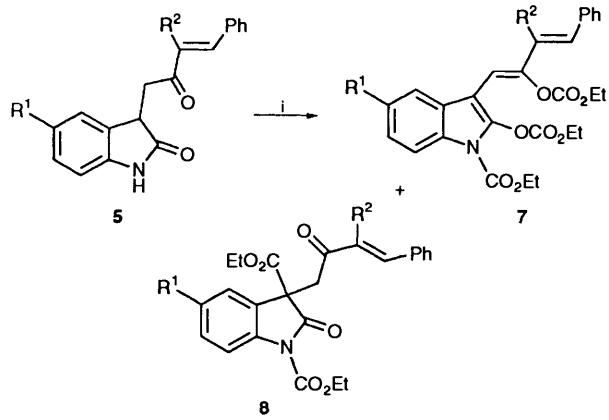
Table 1 Compounds **3**, **4**, **5** and **6** prepared in this work

Starting material	Product[a]	R^1	R^2	Yield (%)	M.p. (T/°C) (Solvent)
1a	**3aa**	H	H	65	161–163 (EtOH)
1a	**3ab**	H	Me	70	146–148 (CH_2Cl_2–Et_2O)
1a	**3ac**	H	Et	70	184–186 (EtOH)
1a	**3ad**	H	Ph	92	191–192 (EtOH)
1b	**3bb**	Cl	Me	75	185–186 (EtOH)
1c	**3cc**	Br	Et	35	189–190 (decomp.) (CH_2Cl_2–Et_2O)
3aa	**4aa**[b]	H	H	95	169–170 (CH_2Cl_2–Et_2O)
3ab	**4ab**[c]	H	Me	87	175–176 (CH_2Cl_2–Et_2O)
3ac	**4ac**[c]	H	Et	94	151–152 (CH_2Cl_2–Et_2O)
3ad	**4ad**[d]	H	Ph	88	190–191 (CH_2Cl_2–Et_2O)
3bb	**4bb**[d]	Cl	Me	45	200–202 (CH_2Cl_2–Et_2O)
3cc	**4cc**[d]	Br	Et	72	199–201 (Et_2O)
4aa	**5aa**	H	H	46	127–129 (Et_2O)
4ab	**5ab**	H	Me	93	122–124 (Et_2O)
4ac	**5ac**	H	Et	76	131–132 (Et_2O)
4ad	**5ad**	H	Ph	55	176–177 (CH_2Cl_2–Et_2O)
4bb	**5bb**	Cl	Me	65	165–166 (CH_2Cl_2–Et_2O)
4cc	**5cc**	Br	Et	83	136–138 (Et_2O–pentane)
3ab	**6ab**	H	Me	95	228–230 (EtOH)
3ac	**6ac**	H	Et	94	206–208 (MeOH)
3ad	**6ad**	H	Ph	95	211–212 (CH_2Cl_2–Et_2O)
3bb	**6bb**	Cl	Me	88	223–225 (CH_2Cl_2–Et_2O)
3cc	**6cc**	Br	Et	85	227–229 (Me_2CO–CH_2Cl_2)

[a] Satisfactory microanalyses obtained: C ± 0.19; H ± 0.12; N ± 0.13%. [b] Method A. [c] Method B. [d] Method C.



Scheme 2 *Reagents:* i, H^+



Scheme 3 *Reagents:* i, Et_3N, $ClCO_2Et$, CH_2Cl_2

acyloins **3** *via* the unsaturated derivatives **4** (Scheme 2) which may add a proton at position 3 and then cyclize by intramolecular nucleophilic attack. During the reaction with HCl–EtOH, transient formation of the deep-red colour typical of compounds **4** was observed. Confirmation of this view is that compounds **6** may also be obtained from enones **4** under the same reaction conditions. The lack of cyclization of compound **3aa** (R^2 = H) to the corresponding spirane derivative may be due to the lack of stabilization of the positive charge at the 10-position of the postulated spiro intermediate. This was confirmed by the extremely easy cyclization of compound **3ad** (R^2 = Ph) whose ring closure to spirane **6ad** occurred by reaction with the HCl evolved by reaction of $SOCl_2$ in CH_2Cl_2.

When compounds **5** were treated with an excess of ethyl chloroformate and triethylamine in CH_2Cl_2 solution at 0 °C, the corresponding 3-(buta-1,3-dienyl)indoles **7** were formed. In the case of compounds **5ab**, **5ac**, **5bb** and **5cc**, besides compounds **7**, derivatives **8** were also obtained (Scheme 3, Table 2). The acylation mechanism responsible for this dualism has already been elucidated for similar derivatives.[9] The reported structures for compounds **7** and **8** are based on analytical and spectroscopic data (Table 4) as well as on their chemical behaviour. Moreover, the structure of compound **7ab** has been confirmed by X-ray diffraction analysis.* Fig. 2 shows the molecular shape and crystallographic numbering scheme. Details of crystallographic data, data collection and structure refinement are reported in Table 5 (see later).

Alkaline hydrolysis of compounds **8**, followed by acidification, gave the spirane derivatives **9**, with evolution of CO_2

* Crystallographic details have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge CB2 1EW, England.

Table 2 Compounds **7** and **8** prepared in this work

Starting material	Product[a]	R^1	R^2	Yield (%)	M.p. (T/°C) (Solvent)
5aa	**7aa**	H	H	95	122–123 (CH_2Cl_2–Et_2O)
5ab	**7ab**	H	Me	54	101–103 (Et_2O–pentane)
	8ab			44	70–72 (pentane)
5ac	**7ac**	H	Et	46	87–89 (Et_2O–pentane)
	8ac			52	89–90 (Et_2O–pentane)
5ad	**7ad**	H	Ph	77	90–92 (Et_2O–pentane)
5bb	**7bb**	Cl	Me	42	94–95 (Et_2O–pentane)
	8bb			55	97–98 (pentane)
5cc	**7cc**	Br	Et	45	110–112 (Et_2O–pentane)
	8cc			37	56–58 (pentane)

[a] Satisfactory microanalyses were obtained: C ± 0.15; H ± 0.12; N ± 0.12%.

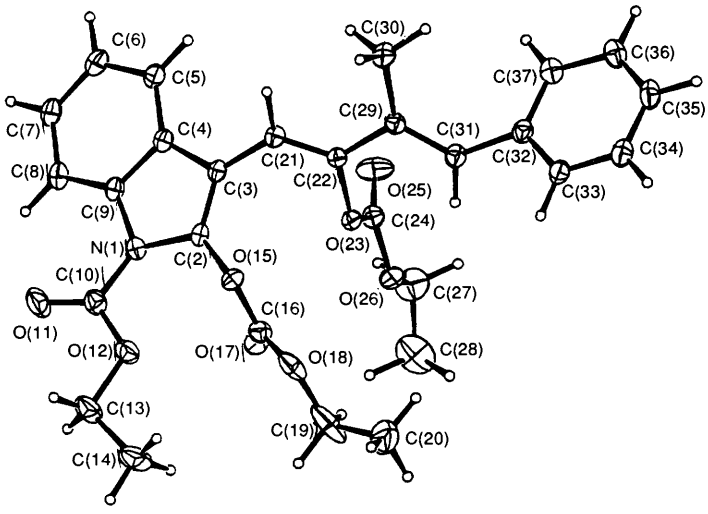
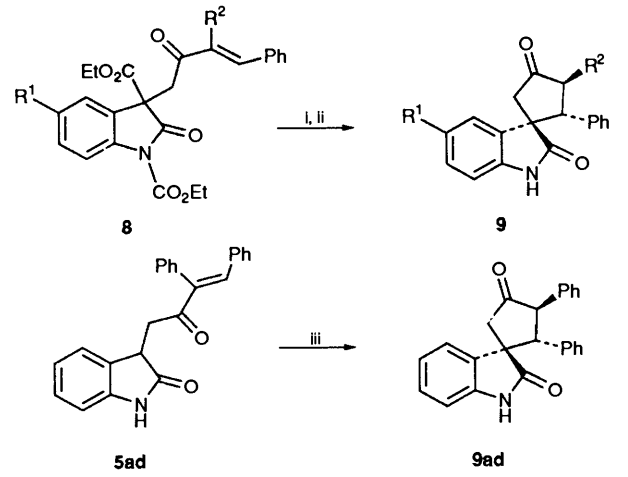


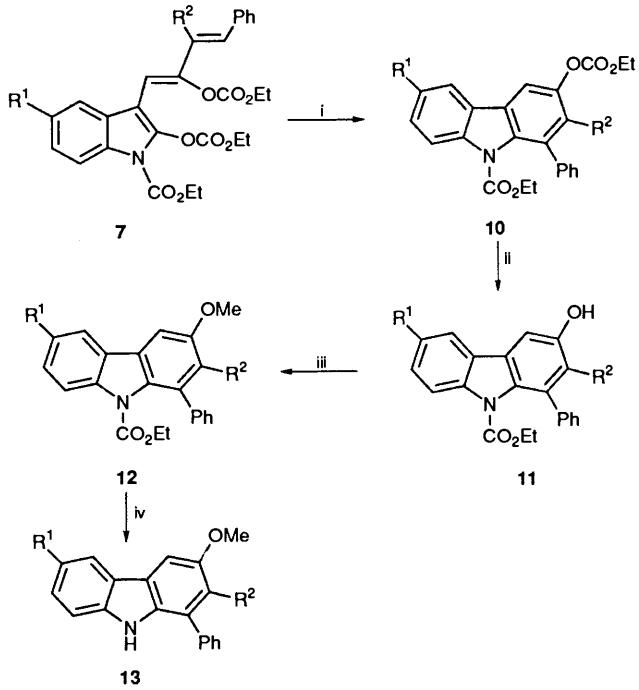
Fig. 2 ORTEP drawing of compound **7ab**, with crystallographic numbering scheme

(Scheme 4, Table 3). This cyclization is explained by intramolecular Michael attack of the carbanionic intermediate produced by hydrolysis of the ester and decarboxylation. In good agreement, the same derivatives **9** may also be obtained from compounds **5** by generation of the same carbanionic intermediate with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in



Scheme 4 *Reagents:* i, OH^-; ii, H^+; iii, DBN, CH_2Cl_2

CH_2Cl_2: compound **9ad** has been obtained by this method from compound **5ad** (Scheme 4, Table 3). The structure of compounds **9** is based on analytical and spectroscopic data (Table 4). The structure of compound **9bb** has been confirmed by X-ray diffraction analysis,† and Fig. 3. shows the molecular shape and the crystallographic numbering scheme. Thermal cyclization of the 3-(buta-1,3-dienyl)indoles **7** gave the corresponding carbazoles **10** (Scheme 5, Table 3). The reported yields are based on the consumed trienes **7**. The ^1H NMR spectra of these compounds **10** give evidence for a shielding effect on the hydrogens of the ethoxycarbonyl group at the 9-position from the phenyl group at the 1-position (OCH_2: δ 3.5–3.6). The steric hindrance due to the phenyl group at the 1-position allows the selective hydrolysis of the carbonate ester at the 3-position. The thus obtained carbazoles **11** were transformed into the methoxy derivatives **12** *via* NaH–THF–MeI. The final derivatives **13** were prepared from **12** *via* alkaline hydrolysis under reflux. Compounds **13ab** and **13bb** are identical with the natural products, hyellazole and 6-chlorohyellazole respectively[5] (Scheme 5, Table 3). Bromination of



Scheme 5 *Reagents and conditions:* i, decalin, reflux; ii, OH^-, aq. MeOH, reflux, 5 min; iii, NaH, MeI, THF; iv, as ii, for 3 h

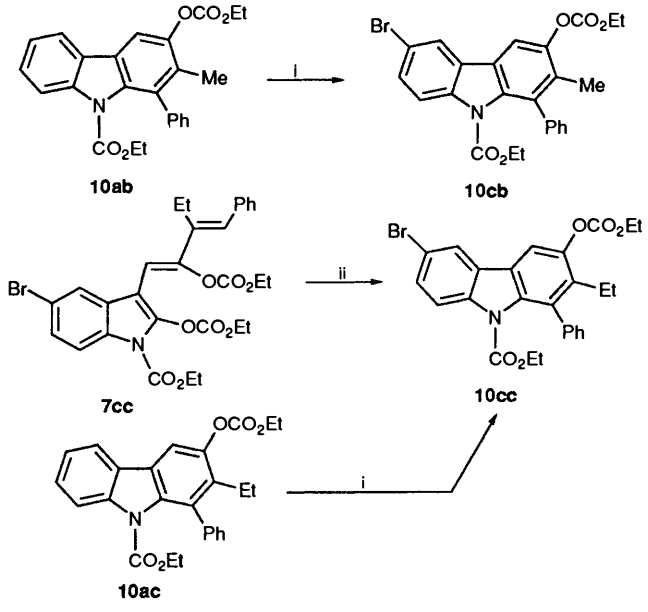
10ab (Br_2 in CH_2Cl_2) afforded compound **10cb** with introduction of the bromine at the 6-position (Scheme 6, Table 3). From bromide **10cb**, compound **13cb** has been obtained following Scheme 5. The position of the bromine atom in

† Crystallographic details have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge CB2 1EW, England.

Table 3 Compounds **9–13** prepared in this work

Starting material	Product[a]	R^1	R^2	Yield (%)	M.p. (T/°C) or b.p. (T/°C)/ pressure (mmHg) (Solvent)
7aa	**10aa**	H	H	58 (28)[b]	238–240/0.2
7ab	**10ab**	H	Me	72 (36)[b]	245–248/0.2
7ac	**10ac**	H	Et	78 (43)[b]	250–255/0.2
7ad	**10ad**	H	Ph	65 (33)[b]	153–155 (Et_2O)
7bb	**10bb**	Cl	Me	83 (35)[b]	48–50 (pentane)
7cc	**10cc**	Br	Et	60 (32)[b]	55–56 (pentane)
8ab	**9ab**	H	Me	64	198 (Et_2O–pentane)
8ac	**9ac**	H	Et	65	168–170 (Et_2O)
8bb	**9bb**	Cl	Me	73	227–229 (Et_2O)
8cc	**9cc**	Br	Et	64	195–196 (CH_2Cl_2–Et_2O)
5ad	**9ad**	H	Ph	71	229–231 (Et_2O)
10ab	**10cb**	Br	Me	85	93–95 (pentane)
10ac	**10cc**	Br	Et	81	55–56 (pentane)
10aa	**11aa**	H	H	72	240–245/0.22
10ab	**11ab**	H	Me	80	245–250/0.22
10ac	**11ac**	H	Et	63	240–245/0.25
10ad	**11ad**	H	Ph	99	134–136 (Et_2O–pentane)
10bb	**11bb**	Cl	Me	88	168–169 (pentane)
10cc	**11cc**	Br	Et	88	158–160 (Et_2O)
10cb	**11cb**	Br	Me	92	156–157 (pentane)
11aa	**12aa**	H	H	76	104 (pentane)
11ab	**12ab**	H	Me	99	142–143 (Et_2O–pentane)
11ac	**12ac**	H	Et	99	88–90 (MeOH)
11ad	**12ad**	H	Ph	96	128 (Et_2O)
11bb	**12bb**	Cl	Me	99	170 (Et_2O)
11cc	**12cc**	Br	Et	99	119–121 (MeOH)
11cb	**12cb**	Br	Me	95	169–170 (pentane)
12aa	**13aa**	H	H	99	240–245/0.2
12ab	**13ab**	H	Me	97	133–134 (Et_2O–pentane)[c]
12ac	**13ac**	H	Et	78	140–142 (pentane)
12ad	**13ad**	H	Ph	98	243 (Et_2O)
12bb	**13bb**	Cl	Me	99	160–161 (MeOH)[d]
12cc	**13cc**	Br	Et	78	118–120 (MeOH)
12cb	**13cb**	Br	Me	95	171–173 (Et_2O–pentane)

[a] Satisfactory microanalyses were obtained: C ± 0.17; H ± 0.11; N ± 0.13%. [b] Unchanged material (%). [c] Lit.,[3] 133–134 °C. [d] Lit.,[3] 163–164 °C.



Scheme 6 *Reagents and conditions:* i, Br_2, CH_2Cl_2; ii, reflux

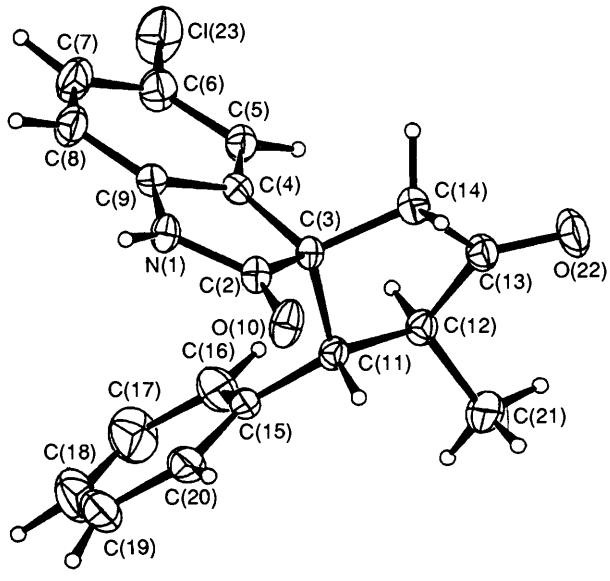


Fig. 3 ORTEP drawing of compound **9bb** (molecule a), with crystallographic numbering scheme

compound **10cb** follows from the ^1H NMR spectrum (Table 4) and from the fact that bromination of compound **10ac** affords compound **10cc**, obtained also from 5-bromoindole-2,3-dione and the ketone **2c** (Scheme 1).

X-Ray Crystallography.—Bond distances and angles, for all three structures, do not present any particular problems, being in agreement with literature data.[10]

Compound **9bb** crystallizes in a monoclinic cell with two

Table 4 Spectral data of compounds **3–13**

Product	IR (Nujol or film, unless stated otherwise) ν/cm^{-1}	^{1}H NMR ($CDCl_3$, unless stated otherwise) δ(J/Hz)
3aa	3380, 3240, 1712, 1668, 1631	3.19 and 3.42 (2 H, AB, 16.70), 4.78 (1 H, s),[a] 6.68 (1 H, d, 16.2), 6.87 (1 H, d, 7.9), 7.00 (1 H, t, 7.5), 7.22 (1 H, t, 7.3), 7.36 (3 H, m), 7.47 (4 H, m), 8.14 (1 H, br s)[a]
3ab	3382, 1719, 1651	2.01 (3 H, s), 3.37 and 3.63 (2 H, AB, 16.9), 4.61 (1 H, s),[a] 6.88 (1 H, d, 7.7), 7.03 (1 H, t, 7.5), 7.26 (1 H, t, 7.8), 7.38 (6 H, m), 7.46 (1 H, s), 7.83 (1 H, br s)[a]
3ac	3300, 1710, 1634, 1619	0.89 (3 H, t, 7.5), 2.36 (2 H, q, 7.5), 3.36 and 3.57 (2 H, AB, 16.7), 5.28 (1 H, s),[a] 6.81 (1 H, d, 7.7), 6.90 (1 H, t, 7.5), 7.13 (1 H, m), 7.24–7.34 (6 H, m), 7.36 (1 H, s), 9.19 (1 H, br s)[a]
3ad	3357, 3200, 1710, 1671, 1619	[$(CD_3)_2SO$] 3.28 and 3.68 (2 H, AB, 17.0), 5.96 (1 H, s),[a] 6.77 (1 H, d, 7.6), 6.88 (1 H, t, 7.5), 6.95–7.04 (4 H, m), 7.14–7.26 (5 H, m), 7.37 (3 H, m), 7.64 (1 H, s), 10.18 (1 H, s)[a]
3bb	3250sh, 3190, 1709, 1696, 1671, 1619	2.03 (3 H, s), 3.36 and 3.64 (2 H, AB, 17.2), 4.42 (1 H, s),[a] 6.81 (1 H, d, 8.3), 7.25 (3 H, m), 7.35–7.43 (5 H, m), 7.47 (1 H, br s)[a]
3cc	3240, 3200, 1701, 1682, 1621	1.05 (3 H, t, 7.5), 2.49 (2 H, q, 7.5), 3.34 and 3.61 (2 H, AB, 17.0), 4.62 (1 H, s),[a] 6.78 (1 H, d, 8.3), 7.33–7.41 (7 H, m), 7.50 (1 H, d, 1.8), 7.80 (1 H, br s)[a]
4aa	3180, 1710, 1669, 1631, 1618	6.83 (1 H, d, 7.8), 7.04 (1 H, t, 7.8), 7.06 (1 H, d, 16.2), 7.32 (1 H, t, 7.7), 7.44 (3 H, m, 2 H after D_2O), 7.49 (1 H, s), 7.61 (2 H, m), 7.76 (1 H, d, 16.2), 8.51 (2 H, d, 7.8)
4ab	3160, 1710, 1650, 1619	2.24 (3 H, s), 6.87 (1 H, d, 7.8), 6.98 (1 H, t, 7.7), 7.27 (1 H, t, 7.7), 7.45 (5 H, m), 7.70 (2 H, s), 7.95 (1 H, d, 7.7), 8.42 (1 H, br s)[a]
4ac	3150br, 1709	1.22 (3 H, t, 7.5), 2.71 (2 H, q, 7.5), 6.84 (1 H, d, 7.8), 6.99 (1 H, t, 7.7), 7.28 (1 H, m), 7.35–7.44 (5 H, m), 7.64 (1 H, s), 7.67 (1 H, s), 7.77 (1 H, br s)[a]
4ad	3160br, 1709, 1661	6.82 (1 H, d, 7.8), 6.99 (1 H, t, 7.5), 7.09 (2 H, m), 7.15–7.33 (6 H, m), 7.42 (3 H, m), 7.51 (1 H, s), 7.80 (2 H, br s, 1 H after D_2O), 8.27 (1 H, d, 7.8)
4bb	3180, 1712, 1649	2.24 (3 H, d, 1.2), 6.78 (1 H, d, 8.3), 7.26 (1 H, dd, 2.1, 8.3), 7.35–7.49 (5 H, m), 7.68 (1 H, br s), 7.76 (1 H, s), 7.82 (1 H br s),[a] 8.04 (1 H, d, 2.1)
4cc	3160br, 1710, 1645	1.23 (3 H, t, 7.5), 2.05 (2 H, q, 7.5), 6.74 (1 H, d, 8.3), 7.35–7.45 (6 H, m), 7.62 (1 H, s), 7.71 (1 H, s), 7.89 (1 H, br s),[a] 8.16 (1 H, d, 1.9)
5aa	3200, 1710, 1701	3.13 (1 H, dd, 8.8, 18.0), 3.51 (1 H, dd, 3.4, 18.0), 4.02 (1 H, dd, 3.4, 8.8), 6.76 (1 H, d, 16.2), 6.87 (1 H, d, 7.9), 6.96 (1 H, t, 7.63), 7.19 (2 H, m), 7.38 (3 H, m), 7.52 (2 H, m), 7.58 (1 H, d, 16.2), 7.96 (1 H, br s)[a]
5ab	3180, 1708, 1679, 1665	2.08 (3 H, d, 1.2), 3.33 (1 H, dd, 8.6, 17.9), 3.66 (1 H, dd, 3.3, 17.9), 3.99 (1 H, dd, 3.3, 8.6), 6.88 (1 H, d, 8.0), 6.98 (1 H, t, 7.8), 7.21 (2 H, m), 7.32–7.41 (5 H, m), 7.54 (1 H, br s), 7.87 (1 H, br s)[a]
5ac	3160br, 1701, 1661	1.09 (3 H, t, 7.5), 2.55 (2 H, q, 7.5), 3.30 (1 H, dd, 8.8, 17.8), 3.64 (1 H, dd, 3.2, 17.8), 4.02 (1 H, dd, 3.2, 8.8), 6.88 (1 H, d, 8.1), 6.98 (1 H, t, 7.8), 7.21 (2 H, m), 7.39 (5 H, m), 7.48 (1 H, s), 8.02 (1 H, br s)[a]
5ad	3170, 1707, 1688	3.03 (1 H, dd, 8.4, 18.5), 3.36 (1 H, dd, 3.3, 18.5), 3.93 (1 H, dd, 3.3, 8.4), 6.84 (1 H, d, 7.6), 7.00 (3 H, m), 7.11–7.23 (7 H, m), 7.39 (3 H, m), 7.69 (1 H, s), 7.86 (1 H, br s)[a]
5bb	3180, 1706, 1670	2.07 (3 H, s), 3.35 (1 H, dd, 8.4, 18.1), 3.68 (1 H, dd, 3.1, 18.1), 3.94 (1 H, dd, 3.1, 8.4), 6.80 (1 H, d, 8.0), 7.18 (2 H, m), 7.32–7.41 (5 H, m), 7.55 (1 H, br s), 7.83 (1 H, br s)[a]
5cc	3160br, 1700, 1658	1.09 (3 H, t, 7.5), 2.55 (2 H, q, 7.5), 3.32 (1 H, dd, 8.5, 17.9), 3.64 (1 H, dd, 3.2, 17.9), 3.98 (1 H, dd, 3.2, 8.5), 6.77 (1 H, d, 8.8), 7.31–7.41 (7 H, m), 7.48 (1 H, s), 8.42 (1 H, br s)[a]
6ab	3320, 1734, 1728, 1693	1.86 (3 H, s), 2.74 and 3.09 (2 H, AB, 18.3), 6.81 (1 H, d, 7.7), 6.88 (2 H, m), 7.07 (2 H, m), 7.21 (4 H, m), 7.87 (1 H, br s)[a]
6ac	3308, 1718, 1700	1.04 (3 H, t, 7.5), 2.25 (2 H, q, 7.5), 2.73 and 3.08 (2 H, AB, 18.3), 6.78 (1 H, d, 7.7), 6.85 (2 H, m), 7.02–7.25 (6 H, m), 7.87 (1 H br s)[a]
6ad	3190, 1705, 1617	2.85 and 3.24 (2 H, AB, 18.3), 6.80 (2 H, m), 6.87 (1 H, d, 7.7), 7.02–7.28 (11 H, m), 8.24 (1 H br s)[a]
6bb	3190, 1730, 1710	1.86 (3 H, s), 2.72 and 3.08 (2 H, AB, 18.3), 6.75 (1 H, d, 8.3), 6.92 (2 H, m), 7.08 (1 H, d, 2.1), 7.17–7.26 (4 H, m), 8.05 (1 H, br s)[a]
6cc	3320, 1720, 1703	1.05 (3 H, t, 7.5), 2.25 (2 H, q, 7.5), 2.70 and 3.05 (2 H, AB, 18.3), 6.69 (1 H, d, 8.3), 6.87 (2 H, m), 7.17–7.25 (4 H, m), 7.32 (1 H, dd, 2.0, 8.3), 8.27 (1 H, br s)[a]
7aa	1784, 1771, 1751	1.21 (3 H, t, 7.1), 1.45 (3 H, t, 7.2), 1.48 (3 H, t, 7.1), 4.18 (2 H, q, 7.2), 4.41 (2 H, q, 7.1), 4.51 (2 H, q, 7.1), 6.34 (1 H, s), 6.76 (1 H, d, 15.8), 6.88 (1 H, d, 15.8), 7.35 (5 H, m), 7.48 (2 H, m), 7.76 (1 H, m), 8.12 (1 H, m)
7ab	1783, 1763, 1748	1.12 (3 H, t, 7.1), 1.47 (3 H, t, 7.1), 1.90 (3 H, t, 7.1), 2.18 (3 H, br s), 4.09 (2 H, q, 7.1), 4.38 (2 H, q, 7.1), 4.47 (2 H, q, 7.1), 6.39 (1 H, br s), 6.90 (1 H, br s), 7.22–7.39 (7 H, m), 7.69 (1 H, m), 8.08 (1 H, m)
7ac	1781, 1763, 1749	1.14 (3 H, t, 7.1), 1.31 (3 H, t, 7.5), 1.41 (3 H, t, 7.1), 1.45 (3 H, t, 7.1), 2.60 (2 H, q, 7.5), 4.09 (2 H, q, 7.1), 4.38 (2 H, q, 7.1), 4.47 (2 H, q, 7.1), 6.38 (1 H, s), 6.86 (1 H, s), 7.22–7.38 (7 H, m), 7.68 (1 H, m), 8.09 (1 H, m)
7ad	1781, 1762, 1749	1.20 (3 H, t, 7.1), 1.41 (3 H, t, 7.1), 1.43 (3 H, t, 7.1), 4.16 (2 H, q, 7.1), 4.36 (2 H, q, 7.1), 4.45 (2 H, q, 7.4), 5.89 (1 H, s), 6.92 (3 H, m), 7.09 (3 H, m), 7.21–7.40 (7 H, m), 7.51 (1 H, m), 8.05 (1 H, d, 8.0)
7bb	1780, 1761, 1747	1.19 (3 H, t, 7.1), 1.44 (3 H, t, 7.1), 1.47 (3 H, t, 7.1), 7.09 (3 H, d, 1.2), 4.14 (2 H, q, 7.1), 4.41 (2 H, q, 7.1), 4.50 (2 H, q, 7.1), 6.33 (1 H, s), 6.94 (1 H, br s), 7.28–7.41 (7 H, m), 7.74 (1 H, d, 2.1), 8.05 (1 H, d, 8.8)
7cc	1781, 1761, 1739	1.17 (3 H, t, 7.1), 1.29 (3 H, t, 7.5), 1.41 (3 H, t, 7.1), 1.44 (3 H, t, 7.1), 2.58 (2 H, q, 7.5), 4.11 (2 H, q, 7.1), 4.37 (2 H, q, 7.1), 4.47 (2 H, q, 7.1), 6.30 (1 H, s), 6.87 (1 H, s), 7.25–7.38 (5 H, m), 7.42 (1 H, dd, 2.1, 8.9), 7.84 (1 H, d, 2.1), 7.97 (1 H, d, 8.9)
8ab	1778, 1741, 1718	1.13 (3 H, t, 7.1), 1.47 (3 H, t, 7.1), 1.91 (3 H, d, 1.2), 3.92 and 4.16 (2 H, AB, 18.2), 4.13 (2 H, q, 7.1), 4.50 (2 H, q, 7.1), 7.12 (1 H, m), 7.19 (1 H, m), 7.31–7.40 (6 H, m), 7.57 (1 H, br s), 7.99 (1 H, d, 8.2)
8ac	1773, 1729, 1658	0.89 (3 H, t, 7.5), 1.12 (3 H, t, 7.1), 1.47 (3 H, t, 7.1), 2.37 (2 H, m), 3.87 and 4.12 (2 H, AB, 18.0), 4.13 (2 H, q, 7.1), 4.49 (2 H, q, 7.1), 7.11 (1 H, t, 7.5), 7.19 (1 H, d, 7.3), 7.36 (6 H, m), 7.50 (1 H, s), 7.98 (1 H, d, 8.2)
8bb	1772, 1732, 1660	1.18 (3 H, t, 7.2), 1.49 (3 H, t, 7.1), 1.95 (3 H, d, 1.2), 3.97 and 4.14 (2 H, AB, 18.3), 4.17 (2 H, m), 4.52 (2 H, q, 7.1), 7.20 (1 H, d, 2.4), 7.32–7.44 (6 H, m), 7.61 (1 H, br s), 7.98 (1 H, d, 8.8)
8cc	1778, 1733, 1644	0.93 (3 H, t, 7.5), 1.16 (3 H, t, 7.1), 1.46 (3 H, t, 7.1), 2.39 (2 H, m), 3.86 and 4.11 (2 H, AB, 18.1), 4.15 (2 H, m), 4.48 (2 H, q, 7.1), 7.32 (1 H, d, 2.1), 7.34–7.43 (5 H, m), 7.46 (1 H, dd, 2.1, 8.7), 7.50 (1 H, s), 7.89 (1 H, d, 8.7)
9ab	3200br, 1740, 1685, 1665	1.15 (3 H, d, 6.8), 2.68 (1 H, dd, 18.6, 1.5), 3.08 (1 H, d, 18.6), 3.13 (1 H, m), 3.57 (1 H, d, 13.7), 6.63 (1 H, d, 7.6), 6.91–7.11 (7 H), m), 7.20 (1 H, d, 7.4), 8.00 (1 H, br s)[a]
9ac	3180br, 1741, 1710	0.85 (3 H, t, 7.5), 1.71 (2 H, m), 2.66 (1 H, dd, 1.6, 18.2), 3.05 (1 H, d, 18.2), 3.08 (1 H, m), 3.74 (1 H, d, 13.5), 6.61 (1 H, d, 7.7), 6.92–7.12 (7 H, m), 7.20 (1 H, d, 7.4), 7.53 (1 H, br s)[a]

Table 4 (*continued*)

Product	IR (Nujol or film, unless stated otherwise) ν/cm^{-1}	^{1}H NMR ($CDCl_3$, unless stated otherwise) δ(J/Hz)
9ad	3300br, 1739, 1711	2.82 (1 H, dd, 1.2, 18.3), 3.29 (1 H, d, 18.3), 4.23 (1 H, d, 13.9), 4.36 (1 H, d, 13.9), 6.63 (1 H, br d, 7.3), 6.95–7.29 (13 H, m, 12 H after D_2O), 7.34 (1 H br d, 6.6)
9bb	3200br, 1750, 1740, 1711, 1685	1.16 (3 H, d, 6.8), 2.68 (1 H, dd, 1.3, 18.6), 3.09 (1 H, d, 18.6), 3.10 (1 H, m), 3.57 (1 H, d, 13.7), 6.55 (1 H, d, 8.3), 6.95 (2 H, m), 7.10 (4 H, m), 7.17 (1 H, d, 2.0), 7.59 (1 H, br s)[a]
9cc	3250br, 1739, 1691, 1670	0.85 (3 H, t, 7.5), 1.71 (2 H, m), 2.64 (1 H, dd, 1.2, 18.3), 3.03 (1 H, d, 18.3), 3.05 (1 H, m), 3.73 (1 H, d, 13.5), 6.52 (1 H, d, 8.3), 6.95 (2 H, m), 7.09 (3 H, m), 7.22 (1 H, dd, 1.9, 8.3), 7.30 (1 H, d, 1.8), 8.10 (1 H, br s)[a]
10aa	1755, 1730	0.89 (3 H, t, 7.1), 1.42 (3 H, t, 7.1), 3.58 (2 H, q, 7.1), 4.35 (2 H, q, 7.1), 7.26 (1 H, d, 2.4), 7.31–7.56 (7 H, m), 7.78 (1 H, d, 2.4), 7.95 (1 H, d, 7.6), 8.17 (1 H, d, 8.3)
10ab	1760, 1732	1.04 (3 H, t, 7.1), 1.43 (3 H, t, 7.1), 2.22 (3 H, s), 3.60 (2 H, q, 7.1), 4.37 (2 H, q, 7.1), 7.31–7.51 (7 H, m), 7.78 (1 H, s), 7.92 (1 H, d, 7.6), 8.01 (1 H, d, 8.3)
10ac	1755,1735	1.05 (6 H, m), 1.43 (3 H, t, 7.1), 2.65 (2 H, q, 7.5), 3.62 (2 H, q, 7.1), 4.37 (2 H, q, 7.1), 7.31–7.49 (7 H, m), 7.78 (1 H, s), 7.91 (1 H, d, 7.4), 7.97 (1 H, d, 8.2)
10ad	1759, 1727	0.97 (3 H, t, 7.1), 1.13 (3 H, t, 7.1), 3.51 (2 H, q, 7.1), 4.08 (2 H, q, 7.1), 7.02 (2 H, m), 7.06–7.21 (8 H, m), 7.38 (1 H, t, 7.3), 7.49 (1 H, m), 7.84 (1 H, s), 7.98 (1 H, d, 7.4), 8.07 (1 H, d, 8.3)
10bb	1763, 1737	1.02 (3 H, t, 7.1), 1.42 (3 H, t, 7.1), 2.19 (3 H, s), 3.58 (2 H, q, 7.1), 4.36 (2 H, q, 7.1), 7.32–7.41 (4 H, m), 7.46 (2 H, m), 7.72 (1 H, s), 7.87 (1 H, d, 2.1), 7.92 (1 H, d, 8.8)
10cb	1752, 1738	1.02 (3 H, t, 7.1), 1.43 (3 H, t, 7.1), 2.19 (3 H, s), 3.58 (2 H, q, 7.1), 4.37 (2 H, q, 7.1), 7.35 (3 H, m), 7.46 (3 H, m), 7.51 (1 H, dd, 2.0, 8.8), 7.71 (1 H, s), 7.87 (1 H, d, 8.8), 8.02 (1 H, d, 2.0)
10cc	1763, 1755, 1739	1.05 (3 H, t, 7.5), 1.07 (3 H, t, 7.2), 1.43 (3 H, t, 7.1), 2.67 (2 H, q, 7.5), 3.65 (2 H, q, 7.2), 4.41 (2 H, q, 7.1), 7.39 (3 H, m), 7.48 (2 H, m), 7.54 (1 H, dd, 2.1, 8.8), 7.76 (1 H, s), 7.88 (1 H, d, 8.8), 8.06 (1 H, d, 2.1)
11aa	3400br, 1730, 1690	0.91 (3 H, t, 7.1), 3.62 (2 H, q, 7.1), 4.98 (1 H, s),[a] 6.99 (1 H, d, 2.5), 7.38 (2 H, m), 7.42 (1 H, d, 2.5), 7.45–7.58 (5 H, m), 7.94 (1 H, d, 8.1), 8.20 (1 H, d, 8.2)
11ab	3400br, 1723, 1695	1.02 (3 H, t, 7.1), 2.23 (3 H, s), 3.59 (2 H, q, 7.1), 4.92 (1 H, s),[a] 7.29–7.49 (8 H, m), 7.85 (1 H, d, 7.2), 8.01 (1 H, d, 8.2)
11ac	3440br, 1725, 1700sh	1.04 (3 H, t, 7.1), 1.12 (3 H, t, 7.5), 2.67 (2 H, q, 7.5), 3.62 (2 H, q, 7.1), 4.91 (1 H, s),[a] 7.28–7.48 (8 H, m), 7.86 (1 H, d, 7.7), 7.98 (1 H, d, 8.2)
11ad	3510,1715	0.95 (3 H, t, 7.1), 3.51 (2 H, q, 7.1), 4.93 (1 H, s),[a] 7.05–7.19 (7 H, m), 7.27–7.38 (4 H, m), 7.47 (1 H, m), 7.61 (1 H, s), 7.97 (1 H, d, 7.5), 8.07 (1 H, d, 8.3)
11bb	3530,1700	1.02 (3 H, t, 7.1), 2.23 (3 H, s), 3.59 (2 H, q, 7.1), 5.04 (1 H, s),[a] 7.31–7.36 (5 H, m), 7.46 (2 H, m), 7.79 (1 H, d, 2.1), 7.93 (1 H, d, 8.8)
11cb	3543, 1703	1.02 (3 H, t, 7.1), 2.23 (3 H, s), 3.58 (2 H, q, 7.1), 4.90 (1 H, s),[a] 7.33 (4 H, m), 7.47 (3 H, m), 7.88 (1 H, d, 8.8), 7.97 (1 H, d, 2.0)
11cc	3500, 1708	1.04 (3 H, t, 7.1), 1.11 (3 H, t, 7.5), 2.66 (2 H, q, 7.5), 3.62 (2 H, q, 7.17), 5.06 (1 H, s),[a] 7.31 (2 H, m), 7.36 (2 H, m), 7.42–7.49 (3 H, m), 7.85 (1 H, d, 8.8), 7.95 (1 H, d, 2.0)
12aa	1724	0.88 (3 H, t, 7.1), 3.59 (2 H, q, 7.1), 3.94 (3 H, s), 7.04 (1 H, d, 2.6), 7.32–7.56 (8 H, m), 7.95 (1 H, d, 7.6), 8.18 (1 H, d, 8.3)
12ab	1719	1.02 (3 H, t, 7.1), 2.21 (3 H, s), 3.58 (2 H, q, 7.1), 3.99 (3 H, s), 7.35–7.45 (8 H, m), 7.94 (1 H, d, 7.3), 8.02 (1 H, d, 8.2)
12ac	1726	1.03 (6 H, m), 2.67 (2 H, q, 7.4), 3.61 (2 H, q, 7.1), 4.00 (3 H, s), 7.31–7.47 (8 H, m), 7.93 (1 H, d, 7.5), 8.01 (1 H, d, 8.2)
12ad	1723	0.95 (3 H, t, 7.1), 3.48 (2 H, q, 7.1), 3.87 (3 H, s), 7.00–7.20 (10 H, m), 7.38 (1 H, t, 7.4), 7.48 (1 H, t, 7.5), 7.54 (1 H, s), 8.00 (1 H, d, 7.6), 8.08 (1 H, d, 8.2)
12bb	1712	1.01 (3 H, t, 7.1), 2.20 (3 H, s), 3.57 (2 H, q, 7.1), 3.98 (3 H, s), 7.31–7.38 (5 H, m), 7.46 (2 H, m), 7.91 (1 H, d, 2.1), 7.94 (1 H, d, 8.8)
12cb	1717	1.01 (3 H, t, 7.1), 2.20 (3 H, s), 3.57 (2 H, q, 7.1), 3.98 (3 H, s), 7.34 (4 H, m), 7.47 (3 H, m), 7.89 (1 H, d, 8.8), 8.05 (1 H, d, 2.0)
12cc	1711	1.04 (6 H, m), 2.65 (2 H, q, 7.4), 3.60 (2 H, q, 7.1), 3.98 (3 H, s), 7.35 (3 H, m), 7.37 (1 H, s), 7.44 (2 H, m), 7.48 (1 H, dd, 2.0, 8.8), 7.86 (1 H, d, 8.8), 8.05 (1 H, d, 2.0)
13aa	(CCl_4) 3470	3.96 (3 H, s), 7.10 (1 H, d, 2.3), 7.22 (1 H, m), 7.44 (3 H, m), 7.56 (3 H, m), 7.69 (2 H, m), 8.06 (1 H, d, 7.8), 8.14 (1 H, br s)[a]
13ab	3400, 3360	2.21 (3 H, s), 4.00 (3 H, s), 7.17 (1 H, m), 7.29 (1 H, m), 7.45 (5 H, m), 7.51 (1 H, s), 7.55 (1 H, m), 7.60 (1 H br s),[a] 8.02 (1 H, d, 7.8)
13ac	3418	1.07 (3 H, t, 7.5), 2.64 (2 H, q, 7.5), 3.99 (3 H, s), 7.16 (1 H, m), 7.31 (2 H, m), 7.40–7.55 (6 H, m), 8.01 (1 H, d, 7.8)
13ad	3300	3.87 (3 H, s), 7.13–7.40 (13 H, m), 7.65 (1 H, s), 7.82 (1 H, br s),[a] 8.08 (1 H, d, 7.8)
13bb	3355	2.20 (3 H, s), 3.98 (3 H, s), 7.21 (1 H, m), 7.26 (2 H, m), 7.39–7.56 (5 H, m), 7.61 (1 H, br s),[a] 7.98 (1 H, d, 2.0)
13cb	3357	2.20 (3 H, s), 3.98 (3 H, s), 7.16 (1 H, d, 8.6), 7.41 (4 H, m), 7.56 (3 H, m), 7.61 (1 H, br s),[a] 8.14 (1 H, d, 2.0)
13cc	3470, 3440	1.06 (3 H, t, 7.4), 2.63 (2 H, q, 7.4), 3.97 (3 H, s), 7.14 (1 H, d, 8.6), 7.39 (3 H, m), 7.44 (1 H, s), 7.52 (4 H, m, 3 H after D_2O), 8.13 (1 H, br s)

[a] Exchanged with D_2O.

molecules in the asymmetric unit; the numbering scheme of the two molecules is the same and chemically equivalent atoms are distinguished by the suffixes a and b. Fig. 3 shows only molecule a, because the two molecules differ very little; their main difference is the angle between the mean-squares-planes through the indole and the phenyl rings; these are 56.5(1) and 68.7(1)° for molecules a and b, respectively. Also significant are the differences in the cyclopentane rings, both with an envelope conformation, but with q (total puckering amplitude)[11] of 0.373(3) and 0.402(3) Å for molecules a and b, respectively. Quite obviously, owing to the presence of the double bond C(11)=C(12) [1.353(2) Å], the cyclopentene ring in compound **6ab** is much more planar, q = 0.095(2) Å; in compound **9bb** the conformation is twisted.

In compound **6ab**, to maximize the conjugation between the π system of the phenyl ring and that of the chain C(11)=C(12)–C(13)=O(22), and to achieve compatibility with the steric hindrance between the phenyl and the methyl groups, the

Table 5 Crystal analysis data

	6ab	**7ab**	**9bb**
Crystal data at room temperature:			
Formula	$C_{19}H_{15}NO_2$	$C_{28}H_{29}NO_8$	$C_{19}H_{16}ClNO_2$
M	289.33	507.54	325.80
Crystal habit[a]	tablet	prism	prism
Crystal size (mm)	0.36 × 0.32 × 0.14	0.30 × 0.24 × 0.24	0.32 × 0.24 × 0.16
Unit-cell determination: setting of angles of 25 reflections			
θ range	12.2–14.6	8.3–15.9	10.8–15.5
	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/c$
Unit-cell dimensions:			
a/Å	8.462(2)	7.528(1)	14.728(3)
b/Å	12.002(2)	17.790(4)	17.718(4)
c/Å	14.545(4)	19.488(4)	14.600(4)
β/°	104.29(3)	95.94(2)	116.22(3)
V/Å^3	1431.5(6)	2595.9(9)	3417.9(2)
Z	4	4	8
D_c (g cm^{-3})	1.343	1.299	1.266
$F(000)$	608	1072.0	1360
μ (cm^{-1})	0.08	0.089	0.229
Experimental data technique: Nonius–CAD4 diffractometer, graphite monochromator, Mo-Kα radiation, $\omega/2\theta$scan			
Scan width:		$\theta = 0.7 + 0.35\tan(\theta)$	
θ limits	2.0, 25.0	1.5, 25.0	2.0, 25.0
h limits	0, 10	0, 8	0, 17
k limits	0, 14	0, 21	0, 21
l limits	−17, 16	−23, 23	−17, 15
No. reflections measured	2512	4551	6011
No. reflections independent	2512	4551	6011
No. reflections observed	1996	3231	2880
Criterion	$I > \sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
	1 standard reflection every 180 min. No variation.		
Refinement:	Full-matrix least-squares on F_o		
No. of reflections	1996	3231	2880
No. of parameters	260	426	544
H-atoms (isotropic)	from difference map		(see text)
Second extinction coefficient (g × 10^{-7})	0.9(1)	3.4(3)	1.7(2)
Δ/σ_{max}	0.00	0.02	0.14
Δ/σ_{mean}	0.00	0.00	0.01
Weighting scheme	$w = 2F_oLp/[\sigma^2(I_o) + (cpl^*I_o)^2]^{\ddagger}$		
cpl	0.03	0.03	0.02
Maximum $\Delta\rho$ peak	0.20	0.17	0.31
Final R	0.049	0.050	0.041
Final R_w	0.049	0.051	0.043
Goodness-of-fit	1.581	1.841	2.140

[a] All three compounds formed colourless crystals.

torsion angle C(12)–C(11)–C(15)–C(16) is −28.7(3)°; the same torsion angle in compound **9bb** is −28.9(5) and −33.0(5)° for molecules a and b, respectively.

The only noticeable aspect of compound **7ab** is the conformation of the butadiene chain C(21)=C(22)–C(29)=C(31): we expected coplanarity of this chain with the indole and the phenyl groups; in contrast, the torsion angles C(2)–C(3)–C(21)=C(22) and C(29)=C(31)–C(32)=C(37) are 46.5(4) and −50.9(4)°, respectively. This is probably due both to packing requirements and to attempts to minimize the intramolecular hindrance between the ethyl carbonate groups.

The crystal structure of compound **9bb** is based on an infinite chain of molecules ...a...b...a^i.b^i ($i = x, \frac{1}{2} - y, -\frac{1}{2} + z$) linked by hydrogen bonds H(1a)···O(10b) and H(1b)···O(10a)^i, with N(1a)···O(10b) and N(1b)···O(10a)^i distances 2.827(3) and 2.767(3) Å, respectively.

Also, compound **6ab** presents an infinite chain of relatively weaker hydrogen bonds, but in this case the engaged oxygen atom is that on the cyclopentane ring; here, N(1)···O(22)^{ii} ($ii = \frac{1}{2} + x, -\frac{1}{2} - y, \frac{1}{2} + z$) is 2.916(3) Å long.

The packing of compound **7ab** shows only weak intermolecular interactions.

Experimental

M.p.s were determined on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 instrument, in Nujol mulls for solids and as liquid films for oils. ^{1}H NMR spectra were recorded on a Bruker AC 300 spectrometer for $CDCl_3$ solutions unless otherwise stated. Column chromatography was performed on Merck Kieselgel 60, 0.063–0.2 mm. Evaporation was carried out under reduced pressure in a rotary evaporator.

Compounds **2b**,[12] **2c**[13] and **2d**[14] were prepared according to the literature procedure.

Condensation of the Indole-2,3-diones **1** *with 4-Phenylbut-3-en-2-ones* **2**: *Preparation of Compounds* **3**.—The indole-2,3-dione **1a** (7.5 g, 50 mmol) and the appropriate ketone **2** (55 mmol) were dissolved in EtOH (150 cm^3) and Et_2NH (1 cm^3) was added. The mixture was stored overnight at room temperature for the preparation of compounds **3aa**, **3ab**, **3ac** and **3ad**. The solid which separated was filtered off, washed with Et_2O (100 cm^3), and crystallized (Table 1). The reaction with indole-2,3-diones **1b** and **1c** was carried out under the same conditions, but in a mixture of EtOH (200 cm^3) and THF (100

cm^3) for 4 days. Compound **3cc** was obtained in a pure state after SiO_2 column chromatography, eluent CH_2Cl_2–acetone (3:1).

Dehydration of Derivatives **3**: *Preparation of Compounds* **4**.—*Method A.* Compound **3aa** (11.73 g, 40 mmol) was suspended in EtOH (100 cm^3) and then 32% aq. HCl (50 cm^3) was added. The mixture was heated to reflux for 2 min. The reaction mixture became a deep-red solution and crystallized. After cooling, and dilution with water (100 cm^3), the mixture was filtered. Crystallization (Table 1) gave pure enone **4aa**.

Method B. Compound **3ab** or **3ac** (20 mmol) was supended in CH_2Cl_2 (100 cm^3) and $SOCl_2$ (10 cm^3) was then added. The mixture was heated to reflux for 4 h. The residue obtained after evaporation of the solvent was crystallized (Table 1).

Method C. Compound **3ad**, **3bb** or **3cc** (20 mmol) was dissolved in anhydrous THF (120 cm^3). Ph_3P (7.87 g, 30 mmol) and CCl_4 (10 cm^3) were then added. The solution was heated to reflux for 2 h (**3ad**), 5 h (**3bb**) or 4 h (**3cc**), respectively. The residue obtained after evaporation of the solvent was purified by SiO_2 column chromatography, eluent CH_2Cl_2–Et_2O (20:1) and was then crystallized (Table 1).

Reduction of Derivatives **4**: *Preparation of Compounds* **5**.—A compound **4** (7 mmol) was dissolved in EtOH (40 cm^3)–THF (30 cm^3). To this solution was then added aq. sodium hydrosulfite (85%; 2.87 g, 14 mmol in 20 cm^3). The mixture was heated at 60 °C for 10 min. After evaporation of the solvent, water (100 cm^3) was added and the mixture extracted with CH_2Cl_2 (2 × 50 cm^3). The organic layer was dried (Na_2SO_4), filtered, and evaporated. SiO_2 column chromatography of the residue [eluent CH_2Cl_2–Et_2O (20:1)] and crystallization (Table 1) gave a pure compound **5**.

Reaction of Compounds **3** *with* HCl–EtOH. *Preparation of Compounds* **6**.—A compound **3** (4 mmol) was suspended in EtOH (30 cm^3) and then 32% aq. HCl (15 cm^3) was added. The reaction mixture was heated to reflux for 20 min. After 5 min the reaction mixture became an orange solution and at the end the colour changed to yellow. The EtOH was evaporated off, water (50 cm^3) was added, and the solid was filtered off. Crystallization afforded the pure corresponding derivative **6** (Table 1).

Reaction of Compound **3ad** *with* $SOCl_2$–CH_2Cl_2. *Preparation of Compound* **6ad**.—Compound **3ad** (1.85 g, 5 mmol) was suspended in CH_2Cl_2 (35 cm^3) and then $SOCl_2$ (3.5 cm^3) was added. The reaction mixture was heated to reflux for 4 h and was then kept overnight at room temperature. The residue obtained after evaporation of the solvent was crystallized from CH_2Cl_2–Et_2O to give pure compound **6ad** (1.67 g, 95%).

Reaction of Compounds **5** *with Ethyl Chloroformate and Triethylamine. Preparation of Compounds* **7** and **8**.—A compound **5** (10 mmol) was dissolved in CH_2Cl_2 (100 cm^3) and then Et_3N (7 cm^3, 50 mmol) was added. The stirred reaction mixture was cooled at 0 °C and a solution of ethyl chloroformate (3.85 cm^3, 40 mmol) in CH_2Cl_2 (15 cm^3) was added. After being warmed to room temperature overnight, the reaction mixture was washed with water (2 × 60 cm^3). The organic layer was dried (Na_2SO_4), filtered, and evaporated. The products were separated by silica gel column chromatography, eluent CH_2Cl_2 for **5ab** and **5ac**; hexane–CH_2Cl_2 (1:1) for **5bb** and **5cc**, and crystallized (Table 2).

Alkaline Hydrolysis of Compounds **8**: *Preparation of Compounds* **9**.—A compound **8** (2 mmol) was dissolved in MeOH (30 cm^3) and then aq. KOH (1 g in 3 cm^3) was added. The solution was heated to reflux for 10 min, evaporated, diluted with water (30 cm^3), acidified with 32% aq. HCl, and filtered. Crystallization gave the corresponding pure compound **9** (Table 3).

Compound **9ad** *from Enone* **5ad**.—Compound **5ad** (353 mg, 1 mmol) was dissolved in CH_2Cl_2 (30 cm^3) and then DBN (1 drop) was added. After 24 h at room temperature the solution was evaporated and the residue was purified by silica gel column chromatography, eluent CH_2Cl_2–Et_2O (40:1) (Table 3).

Cyclization of Compounds **7**. *Preparation of Compounds* **10**.—A compound **7** (4 mmol) was dissolved in decalin (30 cm^3) and the solution was heated to reflux for 48 h. The decalin was distilled off, and the residue was separated by silica gel column chromatography, eluent hexane–CH_2Cl_2 (1:1) and then crystallized or distilled (Table 3).

Compounds **11** *from Compounds* **10**.—A compound **10** (1 mmol) was dissolved in MeOH (20 cm^3) and aq. KOH (0.5 g in 5 cm^3) was added. The solution was heated under reflux for 5 min. The solvent was evaporated off, 4% aq. HCl (20 cm^3) was added, and the mixture was extracted with CH_2Cl_2 (2 × 20 cm^3). The organic layer was dried (Na_2SO_4), filtered, and evaporated. The residue was distilled (Table 3). Slight decomposition was observed in the case of compounds **11aa** and **11ab** and these compounds were obtained pure after silica gel column chromatography, eluent CH_2Cl_2–hexane (2:1) and were used in next step without distillation.

Compounds **12** *from Compounds* **11**.—A compound **11** (1 mmol) was dissolved in anhydrous THF (20 cm^3) and then NaH (2 mmol, 60 mg as 80% suspension) was added. After the mixture had been stirred at room temp. for 10 min, an excess of MeI (1 cm^3) was added. The reaction mixture was stirred at room temp. for 20 min, evaporated, treated with dil. HCl (20 cm^3; 4%) and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered, and evaporated. The residue was crystallized (Table 3).

Compounds **13** *from Compounds* **12**.—A compound **12** (1 mmol) was dissolved in MeOH (30 cm^3)–THF (5 cm^3). Aq. KOH (1 g in 5 cm^3) was then added and the reaction mixture was heated under reflux for 4 h. After evaporation of the solvents, water (50 cm^3) was added and the suspension was extracted with CH_2Cl_2 (2 × 40 cm^3). The organic layer was dried (Na_2SO_4), filtered, and evaporated. Crystallization gave the pure corresponding compound **13** (Table 3).

Bromination of Compounds **10ab** *and* **10ac**; *Compounds* **10cb** *and* **10cc**.—Compound **10ab** or **10ac** (0.5 mmol) was dissolved in CH_2Cl_2 (25 cm^3) and an excess of bromine (0.1 cm^3) was added. After being heated under reflux for 10 min the solution was evaporated, and the residue was purified by silica gel column chromatography, eluent hexane–CH_2Cl_2 (1:1), and was crystallized (Table 3).

Crystal-structure Determination of Compounds **6ab**, **7ab** *and* **9bb**.—Table 5 contains the main crystal-analysis parameters. The centres of mass of the independent molecules of compound **9bb** are related approximately by $\frac{1}{2} + x, \frac{1}{2} - y, z$, but there is no relationship between couples of chemically equivalent atoms. The low ratio between observed and total number of reflections is presumably due, at least in part, to this relationship between the mass centres. We have also examined crystals of compound **9ab**: these are monoclinic, space group $P2_1/c$, a = 14.567(6), b = 17.565(4), c = 13.984 (6) Å, β = 116.88(3)°, Z = 8; that

is, isostructural with compound **9bb**. Owing to the quality of the crystals, to the decay of X-ray intensities as a function of v, and to the ratio of observed/total reflections, which all were even worse than for compound **9bb**, we preferred the latter for X-ray analysis.

Two of the ethyl groups of compound **7ab** have quite high thermal parameters and it was difficult to find some of their H-atoms on the difference Fourier map. H-Atoms bonded to C(19) and C(20) were fixed in calculated positions; thermal parameters of those of C(27) and C(28) were also fixed.

The structures were solved by MULTAN82[15] and were refined by the full-matrix least-squares procedure. For all the structures, secondary extinction parameter g was refined according to ref. 16. Most of the calculations were performed with the SDP program,[17] on a MICROVAX computer. PARST[18] was used for geometrical calculations. Atomic scattering factors were those included in the SDP program. The hydrogen atoms are numbered after their carbon or nitrogen atoms. Thermal ellipsoids of heavy atoms are drawn at the 20% probability level.*

* *Supplementary Publications* (see 'Instructions for Authors', January issue). Tables of atomic coordinates, bond lengths and angles, and torsion angles have been deposited at the Cambridge Crystallographic Data Centre. A table of elemental analyses for compounds **3**–**13** has been deposited at the British Library Lending Division [SUP 56982 (3 pp.)].

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