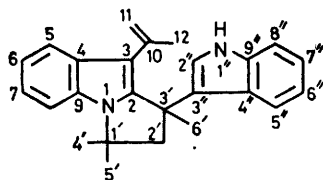


## Lewis-acid-induced Electrophilic Substitution in Indoles with Acetone. Part 2<sup>1</sup>

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The electrophilic substitution reaction of indole with acetone in the presence of boron trifluoride has been followed and the structures of two of the three products isolated have been established. The structure of compound (1), dimer II, was determined by X-ray diffraction methods as crystals from methanol were monoclinic, space group *Cc*, and had cell parameters  $a = 13.383(2)$ ,  $b = 14.064(2)$ ,  $c = 11.638(4)$  Å,  $\beta = 114.74(2)^\circ$ ,  $Z = 4$ . The structure was refined to a final *R* value of 0.068.

We report here the result of our investigation of the electrophilic substitution of indole with acetone in the presence of boron trifluoride. The structures of two of the three products isolated have been established. One of these (dimer II) † exhibited the u.v. absorption characteristic of an indole chromophore; its i.r. spectrum indicated the presence of an indolic NH group (3 420  $\text{cm}^{-1}$ ). The <sup>1</sup>H n.m.r. spectrum revealed the presence of



(1)

nine aromatic protons and an indole NH (10 H, m, *ca.*  $\delta$  6.70–7.70, one disappearing on deuteration), two vinylic protons: C(11) $H_2$ ,  $\delta$  4.90, 4.80 (each 1 H, m), two nonequivalent methylene protons C(2') $H_2$ ,  $\delta$  3.03, 2.55 (each 1 H, d, *J* 13.0 Hz), a vinylic methyl C(12) $H_3$ ,  $\delta$  1.91 (3 H, br s), and three other methyl groups C(5') $H_3$ , C(4') $H_3$ , C(6') $H_3$ ,  $\delta$  1.78, 1.67, 1.51 (each 3 H, s) respectively. This compound afforded a single molecular ion peak at  $M^+$  354 (100%) corresponding to the molecular formula  $C_{25}H_{26}N_2$ .

From the foregoing results and from the crystal structure analysis (see later) the structure for dimer II was established to be as shown in (1) (together with the crystallographic numbering system). An ORTEP drawing is shown in Figure 1.

The compound was found to be unstable when its chloroform solution was warmed and rapidly changed into dimer IIa, compound (3). The formation of the latter was apparent from a study of both <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra of the chloroform solution of dimer II after heating. The important features in the <sup>1</sup>H n.m.r. spectrum were the absence of the signals for the vinylic methylene and methyl groups and the presence of three sharp methyl resonances C(5') $H_3$ , C(4') $H_3$ , and C(6') $H_3$  at

† Dimers I and II refer to the first and second eluted compounds respectively.

$\delta$  2.0, 1.85, and 1.55 (each 3 H, s), and a new peak at  $\delta$  6.25 (1 H, s), the latter being attributed to the indole C(3) $H$ . The remaining portion of the spectrum was similar to that of dimer II.

The <sup>13</sup>C n.m.r. data of dimer IIa confirmed its structure as (3). The assignments are shown in Figure 2. The aromatic protonate carbons appeared as closely spaced lines in the region 122.5 to 110.5 p.p.m.

The formation of dimer II (Scheme 1) is interesting since it involved the dimeric association of the indole ring around three propenic units.

The u.v. absorption spectrum of dimer I is reminiscent of that of substituted indole derivative; its i.r. spectrum showed the presence of the :NH group (3 400  $\text{cm}^{-1}$ ). In

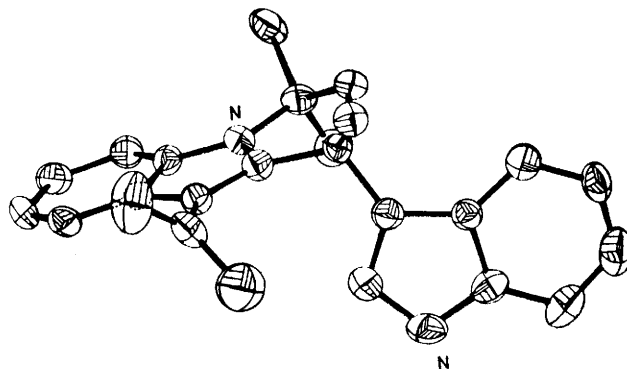


FIGURE 1 ORTEP drawing of dimer II, compound (1). Ellipsoids are shown at the 50% electronic density level

the <sup>1</sup>H n.m.r. spectrum the eight aromatic protons and the indole :NH resonated in the regio *ca.*  $\delta$  6.93–7.54 (9 H, m, one disappearing on deuteration), two vinylic protons at  $\delta$  4.84 and 4.64 (each 1 H, m), a benzylic methylene at  $\delta$  2.74 (2 H, br s), two non-equivalent methylene protons at  $\delta$  3.24 and 2.66 (each 1 H, d, *J* 13.30 Hz), a vinylic methyl at  $\delta$  1.74 (3 H, br s), two tertiary methyls at  $\delta$  1.41 and 1.46 (each 3 H, s), and other two methyl groups at  $\delta$  1.70 and 1.61 (each 3 H, s). In its mass spectrum dimer I showed a single molecular ion peak at  $M^+$  394 (40 a.m.u. higher than for dimer II) corresponding to the molecular formula  $C_{28}H_{30}N_2$  with

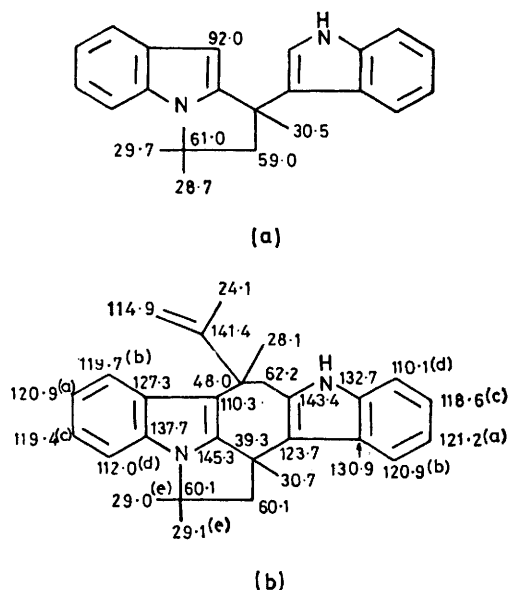
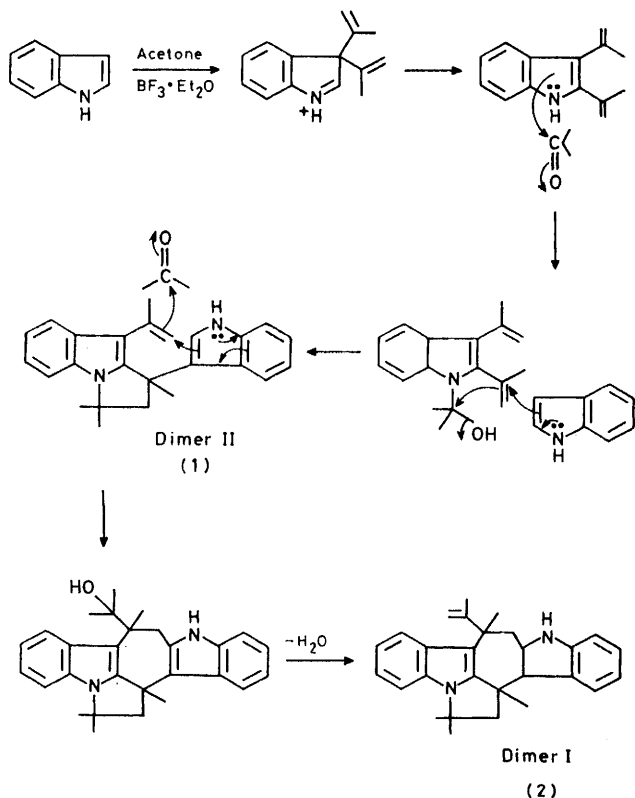


FIGURE 2  $^{13}\text{C}$  N.m.r. resonances (p.p.m.) of (a) dimer IIa, compound (3), and (b) dimer I, compound (2); pairs (a) to (e) may interchange

the base peak at  $m/e$  224 (Scheme 2). Structure (2) thus postulated for dimer I was further corroborated from a  $^{13}\text{C}$  n.m.r. study, the shifts (Figure 2b) being assigned on the basis of their multiplicities.<sup>2</sup>

The formation of dimer I can be explained by the condensation of one molecule of acetone with dimer II



SCHEME 1

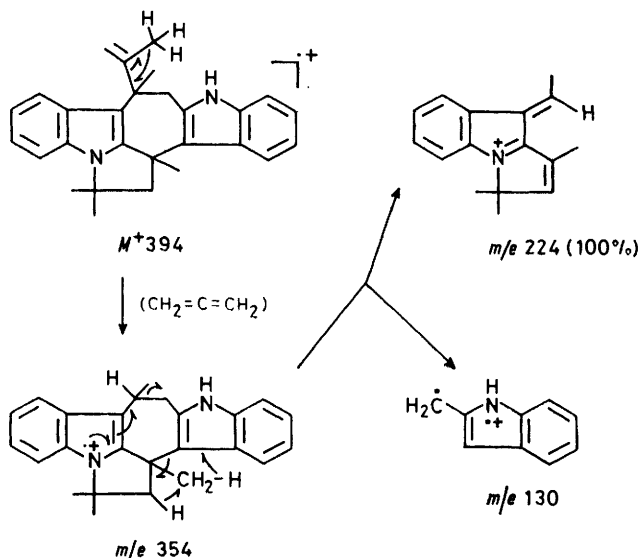
involving the participation of the free C(2'') position and vinylic methylene (Scheme 1).

#### EXPERIMENTAL

M.p.'s were recorded in a Sunvic apparatus. U.v. spectra (95% aldehyde-free ethanol) were recorded on a Carl-Zeiss VSU 1 Universal spectrophotometer, i.r. spectra (KBr disc) on a Beckman IR 20 spectrometer, and n.m.r. spectra on a 80 MHz Varian CFT 20 spectrometer.

The X-ray data for compound (1) recrystallised from methanol were recorded in the  $\theta$ - $2\theta$  mode by use of a Philips PW 1100 automatic four-circle diffractometer with graphite-monochromated Cu- $K_{\alpha}$  radiation. The number of independent reflections above the  $2\sigma$  background level was 1331 ( $2^{\circ} \leq \theta \leq 64^{\circ}$ ). Intensities were corrected for Lorentz and polarization effects but not for absorption.

*Crystal Data.*— $\text{C}_{25}\text{H}_{26}\text{N}_2$ ,  $M = 354$ , monoclinic,  $a = 13.383(2)$ ,  $b = 14.064(2)$ ,  $c = 11.638(4)$  Å,  $\beta = 114.74(2)^{\circ}$ ,



SCHEME 2 Mass spectral fragmentation pattern of dimer I

$U = 2190.487 \text{ \AA}^3$ ,  $D_m = 1.20$ ,  $Z = 4$ ,  $D_c = 1.1817$  Space group  $Cc$ . Cu- $K_{\alpha}$  radiation  $\lambda = 1.5418 \text{ \AA}$ ;  $\mu(\text{Cu-}K_{\alpha}) = 0.0648 \text{ cm}^{-1}$ .

The structure was solved by direct methods<sup>3</sup> (MULTAN) and refined by a full-matrix least-squares procedure with isotropic thermal factors (most of the hydrogen atoms were located on successive Fourier difference maps and included in the subsequent cycles). The final refinements were carried out with anisotropic thermal factors for heavy atoms and led to a conventional  $R$  factor of 0.068. Hydrogen atom parameters were not refined in these last steps. Atom positional co-ordinates are listed in Table 1, bond lengths and angles in Table 2. Final structure factors and thermal parameters are given in Supplementary Publication No. SUP 22592 (11 pp.).\*

*Preparation and Isolation of Dimers I and II.*—To a solution of indole (1 g) in dry methylene chloride (30 ml) at  $0^{\circ}\text{C}$  excess of acetone (30 ml) was added followed by dropwise addition of boron trifluoride etherate (0.5 ml) with stirring. The reaction mixture was kept overnight and then decomposed over ice chips. It was then extracted with

\* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978 Index issue.

TABLE I

Atomic co-ordinates ( $\times 10^4$ ) for the non-hydrogen atoms

Atom	X	Y	Z
N	1 530(4)	202(3)	7 886(5)
C(2)	2 578(5)	412(4)	7 991(6)
C(3)	3 033(5)	-391(4)	7 758(6)
C(4)	2 235(5)	-1 128(4)	7 491(6)
C(5)	2 195(5)	-2 096(4)	7 154(6)
C(6)	1 248(6)	-2 612(4)	6 867(6)
C(7)	308(5)	-2 190(5)	6 917(6)
C(8)	324(5)	-1 245(4)	7 259(6)
C(9)	1 304(5)	-728(4)	7 561(6)
C'(1)	966(5)	1 001(4)	8 188(6)
C'(2)	1 945(5)	1 677(4)	8 828(6)
C'(3)	2 816(5)	1 449(4)	8 283(5)
C'(4)	488(5)	680(5)	9 111(7)
C'(5)	65(5)	1 392(4)	6 978(6)
C'(6)	4 001(5)	1 637(4)	9 290(6)
C(10)	4 165(5)	-518(4)	7 842(6)
C(11)	4 852(6)	-1 217(5)	3 651(9)
C(12)	4 540(7)	87(6)	7 083(9)
N''	2 096(4)	2 422(4)	5 063(4)
C''(2)	2 300(5)	1 684(4)	5 919(6)
C''(3)	2 571(5)	2 035(4)	7 108(6)
C''(4)	2 541(5)	3 047(4)	6 996(6)
C''(5)	2 723(5)	3 808(5)	7 823(6)
C''(6)	2 613(5)	4 726(4)	7 390(7)
C''(7)	2 315(6)	4 916(5)	6 151(10)
C''(8)	2 102(6)	4 205(6)	5 262(8)
C''(9)	2 231(5)	3 269(5)	5 710(6)

methylene chloride, washed (2% NaHCO<sub>3</sub> solution; water), and dried. The concentrated extract was chromatographed over Brockmann alumina (Grade-basic) with solvents of increasing polarity. The dimers were obtained in consecutive fractions on careful chromatographic resolution.

*Dimer I.*—Compound (2), m.p. 230 °C (benzene) was obtained (7%) in the light petroleum (b.p. 60–80 °C) eluate:  $\lambda_{\max}$  (EtOH) (log  $\epsilon$  in parentheses) 230 (4.41), and 382 nm (3.87);  $\lambda_{\max}$  (EtOH: 50% HClO<sub>4</sub>) 228 (4.30), and 270 nm (4.31);  $\nu_{\max}$  (KBr) 3 400, 2 950, 1 630, 1 450, 1 320, 1 300, 1 190, 1 010, 890, and 740 cm<sup>-1</sup>; *m/e* 394 (*M*<sup>+</sup>), 224 (100%) (Found: C, 85.15; H, 7.70; N, 7.15. C<sub>28</sub>H<sub>30</sub>N<sub>2</sub> requires C, 85.24; H, 7.60; N, 7.10%).

*Dimer II.*—Compound (1), m.p. 216–217 °C (benzene) was obtained (6%) in the later fraction of the light petroleum eluate:  $\lambda_{\max}$  (EtOH) 228 (4.48), and 282 nm (3.85);  $\lambda_{\max}$  (EtOH: 50% HClO<sub>4</sub>) 265 nm (4.03);  $\nu_{\max}$  (KBr) 3 420, 2 980, 1 640, 1 410, 1 350, 1 270, 1 180, 1 100, 1 020, 750, and 700 cm<sup>-1</sup>; *m/e*: 354 (*M*<sup>+</sup> 100%); yield: 6% (Found: C, 84.75; H, 7.48; N, 7.95. C<sub>25</sub>H<sub>26</sub>N<sub>2</sub> requires C, 84.70; H, 7.39; N, 7.90).

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TABLE 2

Molecular geometry

(a) Bond lengths (Å)			
N–C(2)	1.388(9)	C'(2)–C'(3)	1.575(9)
N–C(9)	1.360(7)	C'(3)–C'(6)	1.550(9)
N–C'(1)	1.476(8)	C'(3)–C'(3)	1.511(8)
C(2)–C(3)	1.362(8)	C(10)–C(12)	1.458(12)
C(2)–C'(3)	1.502(8)	C(10)–C(11)	1.405(11)
C(3)–C(4)	1.426(9)	N''–C''(2)	1.384(8)
C(3)–C(10)	1.488(10)	N''–C''(9)	1.380(8)
C(4)–C(5)	1.411(8)	C''(2)–C''(3)	1.367(9)
C(4)–C(9)	1.401(10)	C''(3)–C''(4)	1.428(8)
C(5)–C(6)	1.375(10)	C''(4)–C''(5)	1.391(9)
C(6)–C(7)	1.415(11)	C''(4)–C''(9)	1.411(9)
C(7)–C(8)	1.385(9)	C''(5)–C''(6)	1.371(9)
C(8)–C(9)	1.410(10)	C''(6)–C''(7)	1.351(13)
C'(1)–C'(4)	1.529(10)	C''(7)–C''(8)	1.380(12)
C'(1)–C'(5)	1.522(9)	C''(8)–C''(9)	1.400(10)
C'(1)–C'(2)	1.537(9)		
(b) Angles (°)			
C(2)–N–C(9)	109.1(5)	C'(1)–C'(2)–C'(3)	107.7(5)
C(2)–N–C'(1)	114.7(5)	C(2)–C'(3)–C'(2)	99.6(5)
C(9)–N–C'(1)	136.2(5)	C(2)–C'(3)–C'(6)	112.9(5)
N–C(2)–C(3)	109.0(5)	C(2)–C'(3)–C''(3)	112.3(5)
N–C(2)–C'(3)	109.7(5)	C'(2)–C'(3)–C'(6)	110.9(5)
C(3)–C(2)–C'(3)	141.3(6)	C'(2)–C'(3)–C''(3)	109.6(5)
C(2)–C(3)–C(4)	106.9(5)	C'(6)–C'(3)–C''(3)	110.9(5)
C(2)–C(3)–C(10)	127.9(6)	C(3)–C(10)–C(12)	119.3(6)
C(4)–C(3)–C(10)	125.2(6)	C(3)–C(10)–C(11)	119.4(6)
C(3)–C(4)–C(5)	134.4(6)	C(12)–C(10)–C(11)	121.3(7)
C(3)–C(4)–C(9)	107.4(5)	C'(2)–N''–C''(9)	108.3(5)
C(5)–C(4)–C(9)	118.2(6)	N''–C''(2)–C''(3)	110.3(6)
C(4)–C(5)–C(6)	120.0(6)	C'(3)–C''(3)–C''(2)	125.8(6)
C(5)–C(6)–C(7)	120.9(6)	C'(3)–C''(3)–C''(4)	127.8(6)
C(6)–C(7)–C(8)	120.5(6)	C''(2)–C''(3)–C''(4)	106.4(6)
C(7)–C(8)–C(9)	117.8(6)	C''(3)–C''(4)–C''(5)	135.5(6)
N–C(9)–C(4)	107.6(5)	C''(3)–C''(4)–C''(9)	107.6(6)
N–C(9)–C(8)	129.9(6)	C''(5)–C''(4)–C''(9)	116.9(6)
C(4)–C(9)–C(8)	122.4(6)	C''(4)–C''(5)–C''(6)	120.6(6)
N–C'(1)–C'(4)	110.4(5)	C''(5)–C''(6)–C''(7)	121.1(7)
N–C'(1)–C'(5)	109.9(5)	C''(6)–C''(7)–C''(8)	122.2(8)
N–C'(1)–C'(2)	99.7(5)	C''(7)–C''(8)–C''(9)	116.5(8)
C'(4)–C'(1)–C'(5)	110.8(5)	N''–C''(9)–C''(4)	107.5(6)
C'(4)–C'(1)–C'(2)	111.4(5)	N''–C''(9)–C''(8)	129.9(7)
C'(5)–C'(1)–C'(2)	114.1(5)	C''(4)–C''(9)–C''(8)	122.6(6)

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