Addition Reactions of Heterocyclic Compounds. Part XLVII.[1] Formation of Benzazepines from Indoles with Dimethyl Acetylenedicarboxylate in Acetonitrile; Crystal Structure of Dimethyl 2,3-Dihydro-2-indol-3-ylbenz[*b*]azepine-3,4-dicarboxylate

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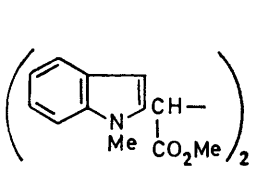
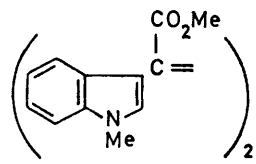
1-Methylindole reacts with dimethyl acetylenedicarboxylate in pure acetonitrile to give dimethyl 1-methylbenz[*b*]azepine-3,4-dicarboxylate. This undergoes a Diels–Alder addition across the 2- and 5-positions with one further mol. equiv. of the acetylene, and with 1-methylindole and acid gives dimethyl 2,3-dihydro-1-methyl-2-(1-methylindol-3-yl)benz[*b*]azepine-3,4-dicarboxylate. Treatment of indole with the acetylenic ester in acetonitrile only gives the corresponding 2,3-dihydro-2-(indol-3-yl)benzazepine (18), the structure of which has been confirmed by an *X*-ray diffraction study. Crystals of (18) are triclinic, a = 10·46, b = 11·50, c = 8·85 Å, α = 91·5, β = 114·6, γ = 106·2, space group $P\bar{1}$. The structure was refined to R 11·4% for 2989 independent reflections. Some reduction products of these azepines are described, and their mode of formation is discussed.

DIELS, ALDER, AND LUBBERT [2] described the formation of the fumarate (6) from 1,2-dimethylindole with dimethyl acetylenedicarboxylate in the absence of solvent, but did not elucidate the stereochemistry. With methanol, as the reaction medium, Johnson [3] obtained the same compound, and the corresponding products from indole and its 1- and 2-methyl derivatives, which he showed were the fumarates. These fumarates gave the corresponding maleates in acetic acid under reflux,[3] or on alumina,[4] and the fumarates were re-formed on irradiation of the maleates in ethanol.[3] Treatment of 1-methylindole with the acetylenic ester in the absence of solvent, however, gave a 2 : 1 molar adduct considered[5] to possess structure (1). This formulation was contested,[6] and independently revised [3] to structure (2), but our new results [7] show that the compound is the benzazepine (9).



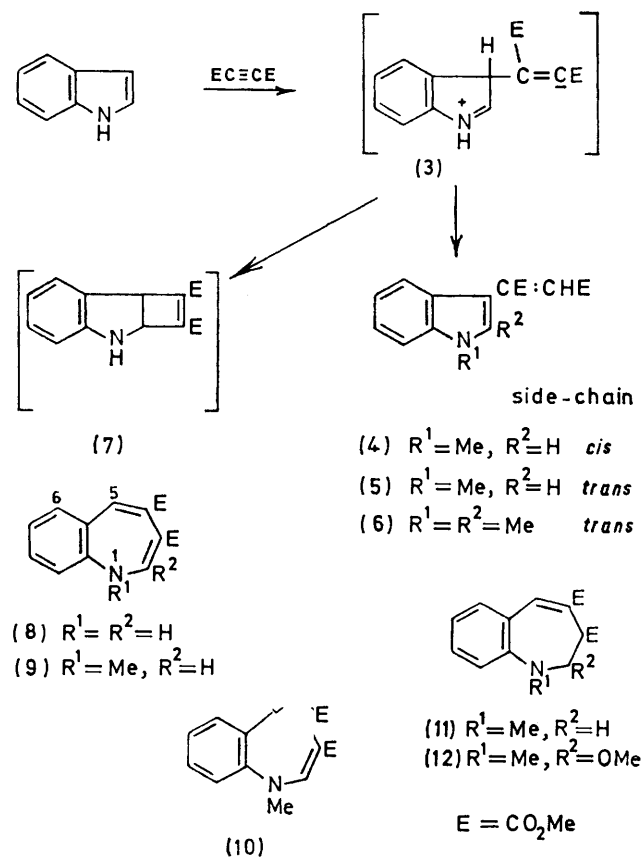
(1)



(2)

In acetonitrile dried with phosphorus pentoxide (a solvent which is not proton-donating and gives relatively little tar in reactions involving dimethyl acetylenedicarboxylate [8]), reaction of the acetylenic ester with 1-methylindole gave a mixture of the benzazepine (9), small quantities of the maleate (4), the fumarate (5), and a minor product (15).

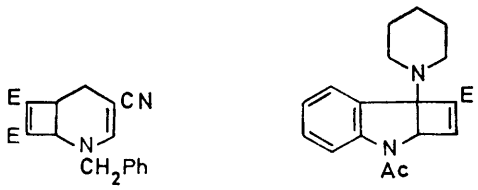
Plieninger and Wild [9] obtained a corresponding 2-ethoxybenzazepine from 2-ethoxy-1-methylindole and the acetylenic ester, and suggested that it was formed *via* a cyclobutene intermediate [*cf.* (7)], which then underwent ring-opening to the benzazepine. The enol ether



system, however, could be at least partially responsible for the reaction as enol ethers undergo similar cyclo-

[1] Part XLVI, R. M. Acheson and J. McK. Woollard, *J. Chem. Soc.* (*C*), 1971, 3296.
[2] O. Diels, K. Alder, and W. Lubbert, *Annalen*, 1931, **490**, 277.
[3] D. C. Johnson, Ph.D. Thesis, University of Minnesota, 1961, see also *Diss. Abs.*, 1962, **23**, 834.
[4] R. W. Campbell, Ph.D. Thesis, University of Minnesota, 1961, see also *Diss. Abs.*, 1962, **22**, 3851.
[5] O. Diels, K. Alder, H. Winkler, and E. Petersen, *Annalen*, 1932, **498**, 1.
[6] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125.
[7] Preliminary report, R. M. Acheson and J. N. Bridson, *Chem. Comm.*, 1971, 1225.
[8] R. M. Acheson, M. W. Foxton, and A. R. Hands, *J. Chem. Soc.* (*C*), 1968, 387.
[9] H. Plieninger and D. Wild, *Chem. Ber.*, 1966, **99**, 3070.

additions.[10] The idea of a cyclobutene intermediate is supported by the formation of compound (13) from 1-benzyl-3-cyano-1,4-dihydropyridine with the ester,[11] and of compound (14), which on heating yields the corresponding benzazepine, from 1-acetyl-3-piperidinoindole with methyl propiolate.[12] In our case of 1-



(13) E = CO_2Me (14)

(15) E = CO_2Me (16) R = OEt (17) R = CN

methylindole, the heterocyclic nitrogen atom and the 2,3-double bond must be behaving as an enamine system, and the concept of the formation of cyclobutenes from enamines *via* a non-concerted process [13] involving zwitterions [*e.g.* (3)] is supported both by the large solvent effect on this type of reaction in particular cases [14] and by the high yields [3] of fumarates [*cf.* (6); 76%] obtained from the indoles and the acetylenic ester in methanol where a proton is available to quench the zwitterion [*e.g.* (3)] as it is formed.

The minor product (15) obtained in the preparation of the benzazepine (9) was also obtained from this benzazepine with an excess of dimethyl acetylenedicarboxylate, and its n.m.r. spectrum (see Table 1) showed two six-proton singlets for the ester methyl groups, indicating the symmetry of the molecule. Cycloadditions of this type have been observed [15] for 1-ethoxycarbonylazepine with tetracyanoethylene and *N*-phenylmaleimide, but no reaction was observed with dimethyl acetylenedicarboxylate, even above 100°.

The benzazepine (9) was stable to attempted catalytic hydrogenation, but reduction with sodium amalgam with methanol and zinc with hydrochloric acid gave compounds (10) and (11), respectively. The u.v. spectrum of the 4,5-dihydrobenzazepine (10) resembled those [16] of the azepines (16) and (17) (see Table 2) and in the n.m.r. spectrum the 4- and 5-protons formed a well defined AMX system. The u.v. spectrum of the 2,3-dihydro-compound (11) is closely similar to those of the methoxy-compound (12) and the indolylbenzazepines (18)—(21).

TABLE 1

N.m.r. spectra (100 MHz; τ values; J in Hz) with internal tetramethylsilane as reference

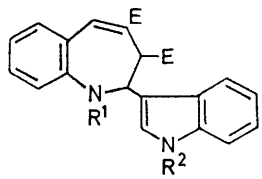
Compd.	Solvent	Proton resonances	Ester methyl groups
(9)	$CDCl_3$	2·5—3·3 (m, Ar-H_4,2- and 5-H), 6·93 (1-Me)	6·20, 6·30
(10)	$CDCl_3$	2·6—3·0 (m, Ar-H_4), 6·52 (1-Me),[a] 2·33 (2-H), 5·76 (q, 4-H), 6·69 (q, $J_{4.5A}$ 5·5, 5-H_A), 6·89 (q, $J_{4.5B}$ 3·0, $J_{5A.5B}$ 13·0, 5-H_B)	6·27, 6·49 [a]
(12)	$CDCl_3$	2·5—3·2 (m, Ar-H_4), 6·92 (1-Me),[a] 4·75 (d, 2-H), 6·73 (2-OMe),[a] 5·33 (d, 3-H), 2·05 (d, $J_{2.3}$ 5·0, 5-H)	6·20, 6·36
(15)	$CDCl_3$	2·68—3·37 (m, Ar-H_4), 5·66 (1-H), 6·72 (8-Me), 4·97 (9-H)	6·11, 6·17 6·19, 6·19
(18)	$(CD_3)_2SO$	2·0—3·5 (m, Ar-H_8, 5-H), 2·49 (d, 1-H),[b] 4·59 (q, 2-H),[c] 5·17 (d, $J_{1.2}$ 6·5, $J_{2.3}$ 4·0, 3-H), −0·62 (1′-H) [b]	6·32, 6·38
(21)	Me_2SO	2·2—3·5 (m, Ar-H_8, 2′-, 5-H), 4·34 (d, 2-H), 5·16 (d, $J_{2.3}$ 4·3, 3-H), 6·50 (1′-Me), 6·69 (1-Me)	6·25, 6·29
(22)	Pyridine	4·20 (q, 2-H),[c] 5·54 (d, 4-CH_2·OH),[g] 5·60—5·80 (m, 3-CH_2·OH),[h] 6·13 (m, 3-H)	
(23) [d]	Pyridine	4·08 (d, 2-H), 5·60 [e] and 5·86,[f] (m, 3-CH_AH_B·OH $J_{HA.HB}$ 10·4), 6·15 (m, $J_{2.3}$ 3·3, $J_{3.HA}$ 4·3, $J_{3.HB}$ 8·8, 3-H), 6·43 (1-Me), 6·96 (1′-Me)	
(24)	$CDCl_3$	2·4—3·2 (m, Ar-H_8), 4·87 (d, $J_{2.3}$ 6·5, 2-H), 6·2—7·1 (m, 3-,4-,5-,5-H_4), 7·14 (1′-Me), 7·21 (1-Me)	6·22, 6·70
(25)	Pyridine	4·54 (d, $J_{2.3}$ 7·5, 2-H), 5·86 and 6·5—7·4 (m, aliphatic H_8), 6·43 (1′-Me), 7·12 (1-Me)	
(26)	Pyridine	5·55 (d, $J_{3a.4}$ 6·5, 4-H), 5·65—6·00 (m, $J_{3HA.3HB}$ 9·6, $J_{3HA.3a}$, $J_{3HB.3a}$ 8·5, 3a-H), 5·97 (t, 3-H_A), 6·26 (t, 3-H_B)	
(27)	$CDCl_3$	0·72 (N−H),[b] 1·47 and 1·70 (vinyl H_2), 2·0—3·4 (m, Ar-H_8, vinyl H_2), 7·07 (NMe_2)	6·32, 6·40

[a] These assignments could be interchanged. [b] Broad, disappears on addition of D_2O. [c] Doublet after addition of D_2O. [d] The spectrum obtained in the presence of D_2O was computer-simulated [26] with the parameters given, and matched the observed spectrum in relative peak intensities and to within ±0·5 Hz for each resonance line. [e] Quartet after addition of D_2O. [f] Triplet after addition of D_2O. [g] Singlet after addition of D_2O. [h] Simplifies after addition of D_2O.

In the presence of hydrochloric acid, which presumably protonates the 3-position, the benzazepine (9) adds

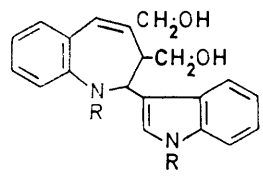
[10] T. W. Doyle, *Canad. J. Chem.*, 1970, **48**, 1629.
[11] R. M. Acheson and N. G. Wright, *Chem. Comm.*, 1971, 1421.
[12] M.-S. Lin and V. Snieckus, *J. Org. Chem.*, 1971, **36**, 645.
[13] R. Hoffman and R. B. Woodward, *Accounts Chem. Res.*, 1968, **1**, 17.
[14] K. C. Brannock, R. D. Burpitt, A. Bell, and C. A. Kelly, *J. Org. Chem.*, 1964, **29**, 801.
[15] A. S. Kende, P. T. Izzo, and J. E. Lancaster, *J. Amer. Chem. Soc.*, 1965, **87**, 5044.
[16] M. Anderson and A. W. Johnson, *J. Chem. Soc.*, 1965, 2411.

methanol, indole, or 1-methylindole to yield respectively the dihydrobenzazepines (12), (20), and (21), which have similar u.v. spectra. The n.m.r. spectra of compounds (12) and (21) show the 2- and 3-proton signals as doublets

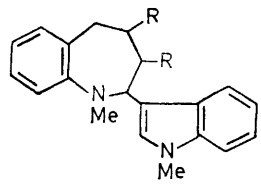


(18) $R^1=R^2=H$
(19) $R^1=H$, $R^2=Me$
(20) $R^1=Me$, $R^2=H$
(21) $R^1=R^2=Me$

$E=CO_2Me$



(22) R = H
(23) R = Me



(24) $R=CO_2Me$
(25) $R=CH_2OH$

TABLE 2

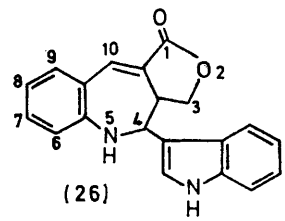
U.v. spectra (methanol) [a]

Compd.	$\lambda_{max.}$/nm ($10^{-4}\varepsilon$)
(9)	*238* (1·56), 260 (2·40), 283 (1·28), *315* (0·38)
(9) [b]	*240* (1·94), 253 (2·48), *281* (1·15), 289 (1·25), *328* (0·30), 373 (0·30)
c	250 (1·92). 282 (1·18), 311 (0·79)
(10)	*234* (0·80), 313 (2·32)
(11)	245 (2·96), 254 (3·17), *263* (2·83), 291 (1·31), *299* (1·16), 387 (0·53)
(12)	*243* (2·64), 252 (3·13), 288 (1·55), *296* (1·40), 371 (0·49)
(12) [b]	253 (2·75), 287 (1·46), *321* (0·36), 271 (0·30)
(15)	*232* (1·75), *261* (0·75), 338 (0·33)
(16)	223 (1·34), 247 (0·48), 310 (1·17)
(17)	229 (1·39), 326 (1·41)
(18)	219 (3·36), *242* (1·85), 255 (2·03), 283 (1·10), 290 (1·10), 390 (0·42)
(19)	223 (4·77), *250* (1·78), 290 (1·01), 380 (0·20)
(20)	220 (4·52), *245* (2·38), 255 (2·58), *283* (1·27), 290 (1·31), *300* (0·95), 394 (0·44)
(21)	227 (2·56), *252* (1·94), 255 (1·96), *282* (0·94), 291 (1·03), 394 (0·43)
(22)	230 (4·04), 274 (1·03), *284* (0·90), *291* (0·64), 335 (0·32)
(22) [b]	240 (1·71), 254 (1·67), *280* (0·90), 288 (0·71)
(23)	230 (4·39), *245* (2·92), 278 (1·12), *283* (0·94), *301* (0·70), 345 (0·35)
(23) [b]	219 (4·41), 255 (1·40), *280* (0·91), *295* (0·50)
(24)	214 (4·07), 224 (4·17), 260 (1·29), 292 (0·84)
(24) [b]	222 (4·03), *275* (0·65), 287 (0·67), *294* (0·65)
(25)	224 (4·00), 245 (1·16), 287 (0·79)
(25) [b]	224 (3·71), *255* (0·63), 267 (0·64)
(26)	219 (4·52), 247 (2·51), 258 (2·78), 283 (1·25), 290 (1·29), *303* (0·90), 395 (0·54)
(27)	225 (3·62), 264 (2·65), 295 (2·09)

[a] Inflection in italics. [b] Acidified with 70% aqueous perchloric acid. [c] Dimethyl 2-ethoxy-1-methylbenz[*b*]azepine-4,5-dicarboxylate.[9]

in the τ 4·3—5·4 region. The adduct (21) is the major product from reaction of 1-methylindole and dimethyl acetylenedicarboxylate in acetonitrile. Its formation is probably due to the presence of small quantities of water, and possibly acid, as the addition of 0·5% of water to our purified acetonitrile again gave this adduct (21) as the main product. The reduction with lithium aluminium hydride of the diester (21) gave the corresponding diol (23), the n.m.r. spectrum of which showed that the methylene protons of the 3-hydroxymethyl group were non-equivalent. Catalytic hydrogenation of this diol gave the tetrahydrobenzazepine (25). Although the diester (21) was stable under these conditions sodium amalgam and methanol reduced the 4,5-double bond, giving compound (24).

Indole and dimethyl acetylenedicarboxylate gave the 2-(indol-3-yl)benzazepine (18) in both purified and untreated acetonitrile. Possibly, the expected 1 : 1 adduct (8) is protonated by indole itself in the absence of other proton sources. The benzazepine (18) was alkylated only on the indolic nitrogen atom by methyl iodide and sodium hydride to give an isomer (19) of compound (20). A suspension of the adduct (18) in ether was stable to lithium aluminium hydride, but with sodium dihydrobis-(2-methoxyethoxy)aluminate in benzene under reflux small quantities of the lactone (26)



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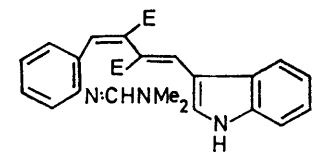

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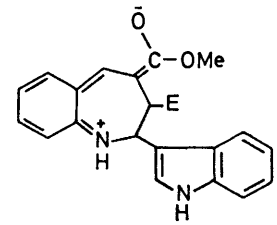

(28) $E=CO_2Me$

and the diol (22) were formed. The lactone possessed a u.v. spectrum similar to that of the original diester (18) showing that the non-conjugated 3-ester group had suffered reduction, an n.m.r. spectrum consistent with the structure proposed, and on reduction with lithium aluminium hydride readily gave the diol. The diol (23) gave tars with tosyl or acetyl chloride and pyridine and with methyl iodide or dimethyl sulphate, and decomposed rapidly in dilute aqueous acid.

The dihydrobenzazepines (18), (20), and (21) were recovered unchanged after attempted dehydrogenation with selenium dioxide or palladised charcoal in decalin under reflux, and bromination gave unstable products or tars. Treatment of the indole derivative (18) with phosphoryl chloride and dimethylformamide,[17] followed

[17] G. Martin and M. Martin, *Bull. Soc. chim. France*, 1963, 1637; W. Jentzsch and M. Seefelder, Ger. P. 1,175,223 (*Chem. Abs.*, 1964, **61**, 13238); K. H. Beyer, H. Eilingsfeld, and H. Weidinger, Ger. P. 1,110,625 (*Chem. Abs.*, 1962, **56**, 3363).

by aqueous potassium hydroxide, gave the indole (27) apparently *via* attack on the azepine nitrogen atom followed by a Hofmann-type elimination. Survival of the amidine group in the basic conditions is perhaps surprising,[18] but some *N*-arylamidines are hydrolysed slowly by bases.[19] The structure of the indole (27) was deduced mainly from the molecular formula and the absence of resonances (excluding OMe) in the saturated C–H region of the n.m.r. spectrum, which indicated the opening of the dihydroazepine ring.

One of the major fragmentations of dihydroazepines in the mass spectrometer is the extrusion of two ring

TABLE 3

Mass spectra; *m/e* values with the % of the base peak in parentheses

Compd.	
(9)	273(87), 272(100), 242(59), 201(43), 200(99), 199(25), 169(39), 155(21), 154(21), 143(39), 131(94), 130(30), 128(26), 121(21), 115(23); *m** 272·5, 199·5, 189·5, 146·5, 130·5, 185, 63
(10)	275(0·9), 274(9), 273(45), 244(5), 243(6), 217(19), 216(100), 184(16), 158(13), 157(62), 156(12), 142(7), 128(7), 115(14); *m** 169·5, 137, 132, 114·5, 106·5, 93
(12)	305(5·7), 274(20), 273(92), 242(17), 214(19), 200(72), 155(14), 154(14), 143(30), 142(13), 140(17), 132(13), 131(100), 130(13), 128(20), 115(19); *m** 189·6, 185, 153·3, 146·5, 129·5, 105, 93, 62·5
(15)	415(70), 384(7), 356(14), 325(23), 324(100), 312(5), 297(18), 265(25), 253(6), 179(5); *m** 305·5, 295, 283, 253, 238
(18)	376(92), 317(64), 285(44), 284(33), 283(32), 259(58), 257(63), 256(46), 232(37), 200(30), 130(32), 129(44), 128(100), 117(51); *m** 315, 267, 255, 209
(21)	406(68), 347(23), 287(31), 286(98), 263(59), 262(100), 226(37), 184(20), 168(22), 158(23), 157(33), 145(22), 144(47), 132(21), 131(34), 130(21), 120(51), 115(17); *m** 314, 233, 225·5, 201·5, 179, 169, 166·5, 157
(22)	348(100), 331(17), 317(23), 299(22), 187(26), 174(32), 158(16), 144(81), 143(17), 131(27)
(23)	350(100), 319(16), 263(15), 262(69), 230(45), 212(48), 200(22), 160(27), 158(23), 145(19), 144(68), 132(38), 131(19), 121(18), 120(40); *m** 315, 291, 260·5, 195·5, 109, 104, 79
(24)	320(90), 302(33), 289(57), 272(32), 271(56), 232(34), 173(38), 160(32), 144(48), 143(40), 130(100), 129(38), 128(36), 117(42); *m** 261, 231, 93·5
(25)	316(100), 272(14), 271(64), 270(11), 269(12), 257(16), 256(20), 143(12), 130(13), 128(16), 117(17)
(26)	431(10), 430(22), 429(14), 372(37), 327(14), 326(10), 325(36), 312(10), 269(11), 268(14), 267(13), 187(17), 186(100), 133(18), 130(16); *m** 429·5, 368·5, 326, 319, 310, 295·5, 266, 200·5, 84·5, 80·5

carbon atoms with their substituents with an apparent contraction to a five-membered ring.[20] Following this pattern, the azepines (18), (21), and (24) lost a fragment corresponding to dimethyl fumarate and compounds (22), (23), and (25) lost a fragment corresponding to $HO{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH$. The azepine (9) also shows the apparent loss of dimethyl acetylenedicarboxylate (confirmed by a metastable ion) to give a very abundant ion.

[18] I. T. Millar and H. D. Springall, 'Sidgwick's Organic Chemistry of Nitrogen,' Clarendon Press, Oxford, 1966.
[19] R. H. de Wolfe, *J. Amer. Chem. Soc.*, 1964, **86**, 864.

An *X*-ray diffraction study of the benzazepine (18) confirmed the structure (see Figure 1) deduced from chemical data. The molecular parameters are shown in

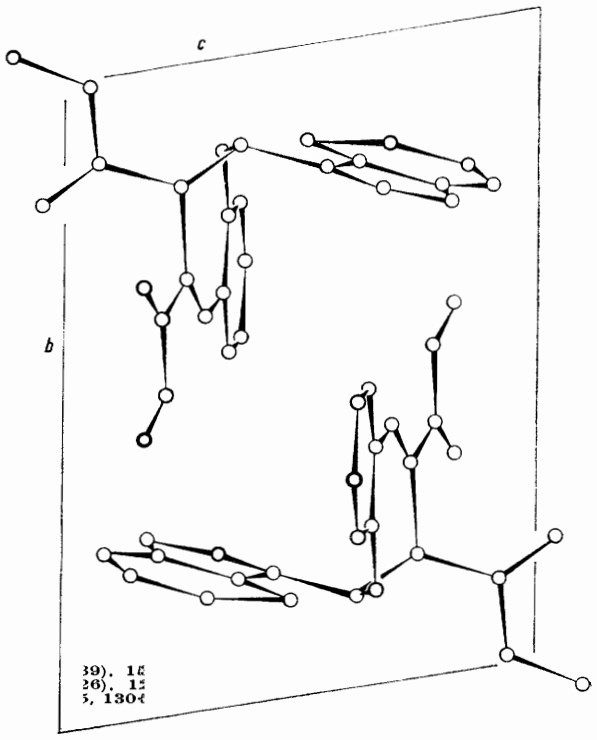

FIGURE 1 Projection of the unit cell of the benzazepine (18) down the *a*-axis

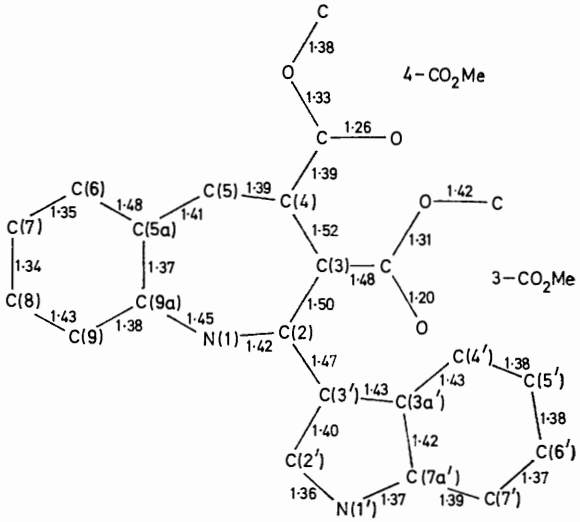

FIGURE 2 The interatomic distances of the benzazepine (18)

Figures 2 and 3. The angles in the seven-membered ring are all larger than expected for a strain-free conformation, the angle at the nitrogen atom (131°) being particularly large. A noteworthy feature is that the N(1),

[20] R. M. Acheson, R. T. Aplin, and D. R. Harrison, *J. Chem. Soc.* (*C*), 1968, 383.

C(4), C(5), C(5a), and C(9a) and the 4-carbonyl group with the associated oxygen atom, are coplanar (see Table 4). Resonance interactions between this carbonyl group and

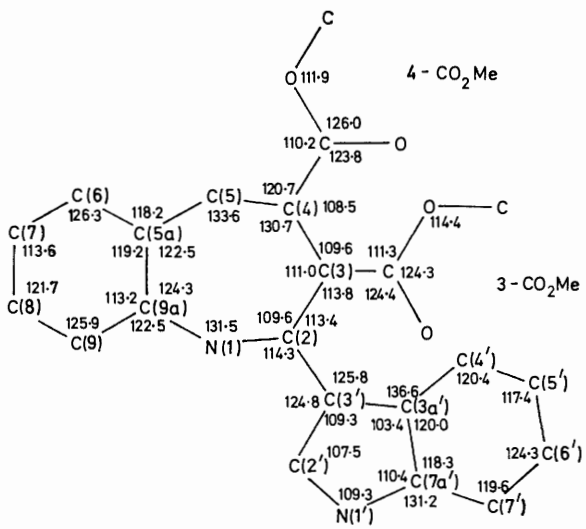

FIGURE 3 The interbond angles of the benzazepine (18)

the lone pair on the nitrogen atom can therefore occur, and the small deviations observed for our compound from the accepted mean bond lengths between carbon, nitrogen, and oxygen atoms are consistent with a contribution from structure (28). This idea also accounts

TABLE 4

Deviations from the least-squares best planes for the three planes involving the atoms for which data is given [a] for the benzazepine (18)

Atom	Deviations (Å)		
N(1)	0·036		
C(2)	0·715 [b]		
C(3)	−0·010 [b]		−0·012
3-$COOCH_3$			0·008
3-$COOCH_3$			0·002
3-$COOCH_3$			0·017
3-$COOCH_3$			−0·014
C(4)	0·054	0·008	
4-$COOCH_3$	0·002	−0·001	
4-$COOCH_3$	−0·047	−0·003	
4-$COOCH_3$	0·005	−0·014	
4-$COOCH_3$	−0·013	0·010	
C(5)	0·061		
C(5a)	−0·026		
C(9a)	−0·072		

[a] The angles between the plane through atoms N(1), C(4), C(5), and C(9a) and the planes through the 3- and 4-CO_2Me groups are 85·8 and 2·3°, respectively. [b] Not included in calculation to determine the plane.

for the facts that (*a*) compounds of this type are not attacked by methyl iodide and methyl sulphate under normal alkylating conditions while the corresponding diols [*e.g.* (22)] are, and (*b*) unlike 2-aminocinnamic acid [21] they do not dissolve in concentrated hydrochloric acid while the diols are sufficiently basic to do so.

EXPERIMENTAL

Instruments and procedures have been described previously.[1] Dimethyl acetylenedicarboxylate was redistilled immediately before use and indole was recrystallised from light petroleum (b.p. 40—60°) (referred to as petrol) and stored *in vacuo* over phosphorus pentoxide. 1-Methylindole, prepared from sodioindole and methyl iodide [22] was freed from indole by heating a 30% solution in xylene under reflux over sodium for 2 days, then removing the solvent *in vacuo*. The residue gave 1-methylindole as an oil, b.p. 117—118° at 18 mmHg, n_D^{20} 1·6060 (lit.,[23] 1·6062).

1-Methylindole and Dimethyl Acetylenedicarboxylate.—1-Methylindole (23·0 g) and the acetylene (17 g) were heated under reflux in acetonitrile (150 ml; previously distilled from phosphorus pentoxide) for 6 days and the solvent was removed by evaporation. Methanol (100 ml) was added and the mixture deposited a red solid on cooling overnight. Recrystallisation gave *dimethyl 1-methylbenz*[b]*azepine-3,4-dicarboxylate* (9) as orange prisms (3·2 g), m.p. 105—107° (from methanol) (Found: C, 66·2; H, 5·6; N, 5·1. $C_{15}H_{15}NO_4$ requires C, 65·9; H, 5·5; N, 5·1%), $\nu_{max.}$ 1730s, 1708s, 1640s, 1594m, and 1574w cm^{-1}. Evaporation of the combined mother liquors gave a red oil, which was chromatographed on alumina (1 kg). Elution with benzene–petrol (1 : 1 v/v; 2·5 l) gave first dimethyl (1-methylindol-3-yl)-fumarate (5) (2·1 g), yellow prisms, m.p. 83—85° (from ether) (lit.,[3] 85—85·5°), followed by *dimethyl 2,3-dihydro-1-methyl-2-(1-methylindol-3-yl)benz*[b]*azepine-3,4-dicarboxylate* (21) (0·39 g), pale yellow plates, m.p. 158—159° (from methanol) (Found: C, 71·2; H, 6·0; N, 6·7. $C_{24}H_{24}N_2O_4$ requires C, 71·3; H, 5·9; N, 7·0%).

Elution with benzene (2·5 l) then gave more azepine (9) (3·7 g) followed by dimethyl (1-methylindol-3-yl)maleate (4) (0·05 g), plates, m.p. 135—137° (from methanol) (lit.,[3] 138—139·5°), and an unidentified yellow solid which crys[illegible]ed from methanol as yellow rods (0·34 g), m.p. 175[illegible]° (Found: C, 60·9; H, 4·6; N, 3·1. $C_{21}H_{19}NO_8$ requires C, 61·0; H, 4·6; N, 3·4%), $\nu_{max.}$ 1750s, 1730s, 1703s, 1622m, 1577w, and 1511s cm^{-1}, $\lambda_{max.}$ 248 (2·50), 290 infl (1·06), 295 (0·28), and 450 (0·55) nm, τ (100 MHz; $CDCl_3$) 2·5—2·9 (4H, m), 3·32 (1H, q, *J* 9·6 and 2·8), 3·91 (q, *J* 9·6 and 2·6), 4·73 (1 H, t, *J* 2·8), 6·05 (3H, s), 6·20 (3H, s), 6·30 (3H, s), and 6·40 (3H, s), *m/e* 413 (M^+, 38%), 412 (43), 382 (14), 381 (7), 366 (7), 353 (22), 354 (100), 308 (6), 295 (10), 244 (6), 237 (22), 179 (21), 178 (13), 177 (5), and 103 (10), *m** 351·5 and 303.

Further elution with benzene gave successively *tetramethyl 8-methyl-8-azatricyclo*[7,2,2,$0^{2,7}$]*trideca-2(7),3,5,10,12-pentaene-10,11,12,13-tetracarboxylate* (15) (0·27 g), yellow rods, m.p. 160—163° (from methanol) (Found: C, 60·7; H, 5·1; N, 3·4. $C_{21}H_{21}NO_8$ requires C, 60·7; H, 5·1; N, 3·4%), $\nu_{max.}$ 1738s, 1720s, 1662w, 1643m, 1606m, and 1571w cm^{-1} and tetramethyl 9-methyl-*trans*-1,2-dihydrocarbazole-1,2,3,4-tetracarboxylate (0·32 g), pale yellow prisms, m.p. 173—175° (from methanol), (lit.,[3] 175—176·5°). Elution with increasingly polar solvents gave trimethyl 5,6-dihydro-5-methyl-6-oxophenanthridine-7,8,9-tricarb-

[21] P. Ruggli and O. Schmid, *Helv. Chim. Acta*, 1935, **18**, 1215.
[22] K. T. Potts and J. E. Saxton, *J. Chem. Soc.*, 1954, 2641.
[23] H. R. Snyder and E. L. Eliel, *J. Amer. Chem. Soc.*, 1948, **70**, 1703.

oxylate (0·15 g), needles, m.p. 169—170° (from methanol) (lit.,[3] 171—172·5).

Treatment of Dimethyl 1-*Methylbenz*[b]*azepine*-3,4-*dicarboxylate with Dimethyl Acetylenedicarboxylate.*—The benzazepine (9) (1·4 g) and the acetylene (0·70 g) were heated at 110° for 3 days. Trituration of the mixture with ether gave the adduct (15) (1·6 g, 75·3%), yellow rods, m.p. and mixed m.p. 161—162° (from methanol).

Reactions of Dimethyl 1-*Methylbenz*[b]*azepine*-3,4-*dicarboxylate* (9).—(i) The azepine (0·5 g) in methanol (50 ml) was stirred with 4% sodium amalgam (10 g) for 2 h and the solution was decanted from remaining amalgam and poured into ice–water (150 ml). The resulting precipitate was recrystallised from methanol to give *dimethyl* 4,5-*dihydro*-1-*methylbenz*[b]*azepine*-3,4-*dicarboxylate* (10) (0·41 g, 81·4%), plates, m.p. 120—120·5° (Found: C, 65·6; H, 6·1; N, 5·0. $C_{15}H_{17}NO_4$ requires C, 65·4; H, 6·2; N, 5·1%), $\nu_{max.}$ 1748s, 1707s, 1623s, 1610m, 1587s, and 1510s cm^{-1}.

(ii) The azepine (9) (0·5 g) was dissolved in a mixture of methanol (50 ml) and aqueous concentrated hydrochloric acid (20 ml); the solution was stirred with zinc dust (2 g) for 30 min and filtered. The filtrate was poured into water (200 ml), the mixture was extracted with ether (3 × 100 ml), and the organic layer was dried ($MgSO_4$) and evaporated to leave a tarry solid. Recrystallisation from methanol gave *dimethyl* 2,3-*dihydro*-1-*methylbenz*[b]*azepine*-3,4-*dicarboxylate* (11) as pale yellow prisms (0·032 g, 6·3%), m.p. 289—290° (Found: C, 65·7; H, 6·3; N, 5·1. $C_{15}H_{17}NO_4$ requires C, 65·4; H, 6·2; N, 5·1%), $\nu_{max.}$ 1750s, 1735s, 1714s, 1703s, 1642m, 1609m, 1563m, and 1509s cm^{-1}.

(iii) The azepine (9) (0·1 g) in a mixture of methtureł (5 ml) and aqueous concentrated hydrochloric acid (5 ml) was poured on crushed ice (20 g) and the red tarry precipitate collected by filtration. Recrystallisation from methanol gave the original azepine (0·03 g) and *dimethyl* 2,3-*dihydro*-2-*methoxy*-1-*methylbenz*[b]*azepine*-3,4-*dicarboxylate* (12), pale yellow rhomboids (0·035 g, 32·4%), m.p. 112—114° (Found: C, 62·9; H, 6·7; N, 4·4. $C_{16}H_{19}NO_5$ requires C, 62·9; H, 6·3; N, 4·6%), $\nu_{max.}$ 1736s, 1704s, 1648s, 1602m, 1561m, and 1501s cm^{-1}.

(iv) The azepine (9) (1·4 g) and 1-methylindole (0·7 g) were heated under reflux in acetonitrile (15 ml) containing aqueous concentrated hydrochloric acid (5 drops) for 1 h. On cooling, the azepine (21) separated as pale yellow prisms (0·9 g, 45·0%), m.p. and mixed m.p. 157—158° (from methanol).

(v) A similar experiment to (iv) with indole gave *dimethyl* 2,3-*dihydro*-2-(*indol*-3-*yl*)-1-*methylbenz*[b]*azepine*-3,4-*dicarboxylate* (20) (1·7 g, 89·4%), m.p. 228—229° (Found: C, 70·5; H, 5·8; N, 7·4. $C_{23}H_{22}N_2O_4$ requires C, 70·7; H, 5·7; N, 7·2%), $\nu_{max.}$ 3360m (broad), 1745s, 1672s, 1649w, 1609m, 1576w, and 1504s cm^{-1}.

Reduction of Dimethyl 1,2-*Dihydro*-1-*methyl*-2-(1-*methylindol*-3-*yl*)*benz*[b]*azepine*-3,4-*dicarboxylate* (21).—(i) Lithium aluminium hydride (0·1 g) was added in small portions with stirring to the azepine (21) (0·4 g) in dry ether (50 ml). After stirring for 3 h, excess of hydride was destroyed with methanol, water (50 ml) was added, and the mixture was extracted with ether (3 × 50 ml). Evaporation of the dried ($MgSO_4$) extract and recrystallisation of the residue from benzene gave 2,3-*dihydro*-2-(1-*methylindol*-3-*yl*)-1-*methylbenz*[b]*azepine*-3,4-*diyldimethanol* (23) (0·23 g, 66·7%) as needles, m.p. 172—173° (Found: C, 75·7; H, 6·9; N, 8·1. $C_{22}H_{24}N_2O_2$ requires C, 75·8; H, 6·9; N, 8·0%), $\nu_{max.}$ 3270m (broad), 1591m, and 1555w cm^{-1}.

The compound (24) (0·4 g) in methanol (200 ml) was shaken with 5% palladium–charcoal (0·2 g) for 3 h under hydrogen (3 atm). Filtration, evaporation, and recrystallisation gave 2,3,4,5-*tetrahydro*-1-*methyl*-2-(1-*methylindol*-3-*yl*)*benz*[b]*azepine*-3,4-*diyldimethanol* (25), prisms (0·26 g, 65·0%), m.p. 165—168° (Found: C, 75·5; H, 7·2; N, 7·8. $C_{22}H_{26}N_2O_2$ requires C, 75·4; H, 7·5; N, 8·0%), $\nu_{max.}$ 3410m (broad), 1608m, and 1586m cm^{-1}.

(ii) Sodium amalgam (4%; 5·0 g) was stirred with the azepine (21) (0·2 g) in methanol (100 ml) overnight. The solution was filtered and evaporated and the residue was recrystallised from acetonitrile to give *dimethyl* 2,3,4,5-*tetrahydro*-2-(1-*methylindol*-3-*yl*)-1-*methylbenz*[b]*azepine*-3,4-*dicarboxylate* (24) (0·14 g, 69·6%), plates, m.p. 188—190° (Found: C, 70·7; H, 6·5; N, 7·1. $C_{24}H_{26}N_2O_4$ requires C, 70·9; H, 6·4; N, 6·9%), $\nu_{max.}$ 1732s, 1602m, 1580w, and 1557w cm^{-1}.

Treatment of Indole with Dimethyl Acetylenedicarboxylate in Acetonitrile.—Indole (23·0 g) and dimethyl acetylenedicarboxylate (14·0 g) were heated under reflux in acetonitrile (100 ml) for 6 days. The solvent was evaporated off and methanol (100 ml) added. After 2 days at 0° the precipitate was recrystallised from methanol to give *dimethyl* 2,3-*dihydro*-2-(*indol*-3-*yl*)*benz*[b]*azepine*-3,4-*dicarboxylate* (18) (6·4 g) as pale yellow prisms, m.p. 240—242° (Found: C, 70·1; H, 5·2; N, 7·3. $C_{22}H_{20}N_2O_4$ requires C, 70·2; H, 5·3; N, 7·5%). The combined evaporated mother liquors were chromatographed on alumina (1·2 kg); elution with benzene (1·5 l) gave, first, *tetramethyl* 9-(trans-1,2-*dimethoxycarbonylethyl*)-1,2-trans-*dihydrocarbazole*-1,2,3,4-*tetracarboxylate* (3·8 g), m.p. 165—169° (from methanol) (Found: C, 57·6; H, 4·8; N, 2·8. $C_{26}H_{25}NO_{12}$ requires C, 57·5; H, 4·6; N, 2·6%), followed by dimethyl indol-3-ylfumarate (0·3 g), m.p. 106—108° (from ether) (lit.,[4] 109—110°). Elution with benzene–ether (9 : 1 v/v, 1 l) gave more azepine (18) (5·0 g), m.p. 242—244°. Further elution with increasingly polar solvents gave, first, tetramethyl carbazole-1,2,3,4-tetracarboxylate, fine yellow needles (6·1 g), m.p. 178—180° (from methanol) (lit.,[24] 182—182·5°), and then trimethyl 5,6-dihydro-6-oxophenanthridine-7,8,9-tricarboxylate (1·3 g) m.p. 276—278° (from acetonitrile) (lit.,[4] 271—272°).

The azepine (18) (5·27 g) in benzene (100 ml) was heated under reflux whilst sodium dihydrobis(2-methoxyethoxy)-aluminate (70% in benzene; 15 ml) was added dropwise. After reflux for 30 min, methanol was added until evolution of hydrogen ceased. Water (50 ml) was added and the mixture was extracted with ether (5 × 100 ml). The organic layer was dried ($MgSO_4$) and evaporated, and the residue, dissolved in methanol (20 ml), was cooled for 30 days. The solid precipitate was recrystallised from methanol to give 3,3a,4,5-*tetrahydro*-4-(*indol*-3-*yl*)*benzo*[b]*furo*[3,4-e]*azepin*-1-*one* (26) (0·12 g, 2·7%) as yellow microcrystals, m.p. 215—217° (Found: C, 75·8; H, 5·1; N, 9·0. $C_{20}H_{16}N_2O_2$ requires C, 75·9; H, 5·1; N, 8·9%), $\nu_{max.}$ 3390m, 3330m, 1725s, 1650s, 1604m, 1570m, and 1510w cm^{-1}. The mother liquors on cooling for 7 days, gave 2,3-*dihydro*-2-(*indol*-3-*yl*)*benz*[b]*azepine*-3,4-*diyldimethanol* (22) (20 mg), yellow rods, m.p. 195—197°, $\nu_{max.}$ 3400s, 3260s,br, 1659w, 1620w, 1600m, and 1573w cm^{-1}.

The lactone (26) (50 mg) in ether (10 ml) was stirred with lithium aluminium hydride (50 mg) for 1 h at room temperature. Methanol was added until evolution of hydrogen

[24] W. E. Noland, W. C. Kuryla, and R. F. Lange, *J. Amer. Chem. Soc.*, 1959, **81**, 6010.

ceased, followed by water (10 ml), and the mixture was extracted with ether (3 × 20 ml). The organic layer was dried ($MgSO_4$) and evaporated and the residue was recrystallised from methanol to give the diol (22) (8 mg, 15·8%) m.p. and mixed m.p. 193—197°.

The azepine (18) (2·1 g) in dimethylformamide (10 ml) was added dropwise with stirring to a solution of phosphoryl chloride (1·0 g) in dimethylformamide (30 ml). The mixture was stirred at room temperature overnight and poured on crushed ice (100 g). The solution was made basic with aqueous 20% potassium hydroxide and slowly warmed to reflux temperature, with gradual addition of more base to maintain the alkalinity. The precipitate was filtered off and recrystallised from methanol to give *dimethyl* 1-[2-(NN-*dimethylamidino*)*phenyl*]-4-(*indol*-3-*yl*)*buta*-1,3-*diene*-2,3-*dicarboxylate* (27) (2·2 g, 91·4%) as pale yellow microcrystals, m.p. 152—154° (Found: C, 69·6; H, 5·8; N, 9·8. $C_{25}H_{25}N_3O_4$ requires C, 69·6; H, 5·8; N, 9·7%), $\nu_{max.}$ 3320s, 1695s, 1640s, 1604m, 1593m, 1568w, and 1513w cm^{-1}.

Determination of the Crystal and Molecular Structure of Dimethyl 2,3-*Dihydro*-2-(*indol*-3-*yl*)*benz*[b]*azepine*-3,4-*dicarboxylate* (18).—*Crystal data.* $C_{22}H_{20}N_2O_4$, $M = 376·4$. Crystals grown from slowly evaporating acetonitrile solutions were triclinic prisms elongated in the *a*-direction: $a = 10·46$, $b = 11·50$, $c = 8·85$ Å, $\alpha = 91·5$, $\beta = 114·6$, $\gamma = 106·2$, $U = 983·2$ Å^3, $D_m = 1·31$ (by flotation in benzene–carbon tetrachloride), $Z = 2$, $D_c = 1·36$, $F(000) = 396$, space group $P\bar{1}$, $\mu = 15·7$ cm^{-1}.

Structure determination. 2989 Independent reflections from a crystal, *ca.* 1·5 × 1 × 1 mm, mounted about the [100] axis, were recorded with Cu-K_α radiation (λ 1·5418 Å) by the equi-inclination, multiple-film Weissenberg technique up to and including the eighth layer. A Weissenberg photograph of the zero layer of the same crystal mounted about the [010] axis was taken to permit correct indexing. Reflections on different film packs were scaled initially on the basis of exposure times and later optimised during structure refinement. The intensities were estimated visually and corrected for Lorentz and polarisation effects but not absorption.

When the overall scale factor and temperature factor had been obtained from a Wilson plot,[25] the symbolic addition program (written by O. J. R. Hodder) was used to derive a trial structure. The signs of 390 reflections with $E > 1·3$ were determined and an *E*-map was computed from which all non-hydrogen atoms were located.

449 Unobserved reflections were removed and the trial structure, with individual isotropic temperature factors, was refined by the least-squares method. After three cycles the *R* factor was 19·3%. Scale factors for each film pack were then refined by two cycles of a least-squares procedure and the positions of hydrogen atoms, other than those in the two methyl groups, were calculated setting C–H and N–H bond lengths at 1·1 and 1·0 Å respectively. Hydrogen temperature factors were set equal to those of the bonded heavy atoms. Inclusion of these data in a further two cycles of least-squares refinement of positional and isotropic temperature factors for heavy atoms, omitting reflections

TABLE 5

Crystallographic data for compound (18) [a]

	Atomic positions in fractional co-ordinates [b]			Anisotropic temperature factors for heavy atoms [c]					
Atom	*x/a*	*y/b*	*z/c*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	0·28453(53)	0·14230(44)	0·33328(63)	200(30)	356(25)	464(27)	177(41)	349(43)	025(38)
N(1′)	0·36929(70)	0·72618(54)	0·17986(61)	645(40)	545(33)	231(23)	089(43)	408(50)	411(57)
C(2)	0·43033(62)	0·13927(48)	0·37481(64)	269(35)	288(25)	270(25)	200(39)	249(44)	183(42)
C(3)	0·48044(58)	0·19528(46)	0·24943(58)	192(29)	306(25)	209(22)	120(37)	232(40)	185(40)
C(4)	0·49768(56)	0·33167(43)	0·26219(57)	165(28)	275(24)	219(22)	152(35)	292(39)	211(39)
C(5)	0·41921(61)	0·39654(48)	0·30103(65)	247(33)	288(25)	285(25)	129(39)	287(45)	131(44)
C(5a)	0·29453(62)	0·36180(51)	0·33637(64)	217(32)	375(28)	249(25)	143(41)	212(42)	112(45)
C(6)	0·22808(75)	0·45623(62)	0·35210(76)	384(41)	506(36)	352(30)	205(52)	354(54)	422(58)
C(7)	0·10492(78)	0·43826(73)	0·37504(85)	327(43)	753(49)	439(35)	217(65)	436(62)	537(70)
C(8)	0·04227(77)	0·32163(76)	0·38368(83)	299(40)	789(52)	399(35)	153(65)	323(59)	295(69)
C(9)	0·10527(67)	0·22786(66)	0·37281(80)	153(36)	666(44)	401(32)	155(57)	236(51)	080(57)
C(9a)	0·22972(65)	0·24327(55)	0·34730(66)	242(35)	443(32)	250(26)	141(45)	208(45)	113(49)
C(2′)	0·49531(76)	0·76159(61)	0·32724(74)	419(40)	500(35)	319(29)	251(50)	402(55)	331(57)
C(3′)	0·46198(63)	0·80919(48)	0·44888(63)	302(34)	313(26)	253(24)	203(39)	321(45)	211(44)
C(3a′)	0·31053(68)	0·80725(50)	0·37162(63)	404(38)	342(27)	200(23)	186(40)	315(47)	114(48)
C(4′)	0·21426(77)	0·84642(65)	0·42252(79)	417(42)	572(39)	361(31)	342(55)	380(60)	309(62)
C(5′)	0·06987(80)	0·83072(84)	0·30835(95)	284(41)	971(60)	526(41)	564(79)	443(65)	412(74)
C(6′)	0·02394(87)	0·77655(85)	0·14509(99)	373(47)	896(61)	503(43)	464(81)	225(69)	097(78)
C(7′)	0·11195(90)	0·73768(75)	0·09056(87)	545(52)	662(47)	349(34)	193(63)	151(65)	−038(74)
C(7a′)	0·25867(74)	0·75400(57)	0·20228(72)	447(40)	426(32)	274(27)	151(47)	311(52)	128(55)
3-$COOCH_3$	0·38219(65)	0·13361(49)	0·07302(66)	318(34)	287(26)	294(27)	035(42)	207(47)	217(45)
3-$COOCH_3$	0·67314(76)	0·81509(47)	0·04092(61)	1176(50)	418(28)	332(24)	120(42)	−226(56)	379(60)
3-$COOCH_3$	0·36221(53)	0·01537(37)	0·05793(50)	604(30)	329(21)	274(19)	−017(31)	238(39)	204(39)
3-$COOCH_3$	0·73522(98)	0·05041(69)	0·10666(89)	809(59)	449(38)	365(35)	−423(59)	113(71)	016(74)
4-$COOCH_3$	0·60691(62)	0·39009(47)	0·21359(61)	256(32)	298(25)	250(24)	069(38)	346(44)	276(43)
4-$COOCH_3$	0·67978(52)	0·33590(39)	0·17204(57)	476(29)	426(23)	514(25)	187(39)	721(46)	207(41)
4-$COOCH_3$	0·62129(48)	0·50901(36)	0·21705(55)	370(25)	336(20)	547(25)	302(36)	653(41)	137(35)
4-$COOCH_3$	0·73165(79)	0·57089(64)	0·17354(93)	405(41)	518(38)	613(42)	516(64)	623(66)	−075(59)

[a] The temperature factor *T* is exp $[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + U_{12}hka^*b^* + U_{13}hla^*c^* + U_{23}klb^*c^*]$. [b] Estimated standard deviations (× 10^5) in parentheses. [b] Temperature factor (× 10^4), estimated standard deviation (× 10^4) in parentheses.

449 Unobserved reflections were removed and the trial structure, with individual isotropic temperature factors, was refined by the least-squares method. After three cycles the *R* factor was 19·3%. Scale factors for each film pack were then refined by two cycles of a least-squares procedure and the positions of hydrogen atoms, other than those in the two methyl groups, were calculated setting C–H and N–H bond lengths at 1·1 and 1·0 Å respectively. Hydrogen temperature factors were set equal to those of the bonded heavy atoms. Inclusion of these data in a further two cycles of least-squares refinement of positional and isotropic temperature factors for heavy atoms, omitting reflections

[25] A. J. C. Wilson, *Acta Cryst.*, 1949, **2**, 318.
[26] C. L. Wilkins and C. E. Klopfenstein, *J. Chem. Educ.*, 1966, **43**, 10; translated into Egtran by P. C. Bell, Part II, Thesis, Oxford, 1967.

suffering from obvious extinction effects, reduced the R factor to 16·1%.

Anistropic temperature parameters were introduced for all heavy atoms and after four cycles of least-squares refinement the R factor was 11·4%. Final positional and anisotropic temperature factors appear in Table 5. A projection of the unit cell down the a-axis is shown in Figure 1. Interatomic distances and interbond angles appear in Figures 2 and 3. The estimated standard deviations of the interatomic distances and interbond angles are in the range 0·008—0·014 Å and 0·6—0·9°, respectively.

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