N(1)—C(2) differ significantly. All these bonds in molecule *A* are significantly longer than those in molecule *B*. The average bond lengths in the aziridine ring of (II) are similar to those of (I). In (I) the non-bonded intramolecular N(1)···N(4) distances of the two molecules are significantly different.

The corresponding bond lengths around the benzoquinone ring of crystallographically independent molecules in (II) and mitomycin C are rather variable. This implies that the electronic character around the ring is relatively easily influenced by the environment. However, it is useful to average the corresponding bond lengths of independent molecules in (II) and mitomycin C and compare them in order to understand the effect of substituent groups at the C(7) position [*O*-methyl and amino group in (II) and mitomycin C, respectively] on the electronic character of the benzoquinone ring. The comparison reveals that in (II) bonds C(6)—C(7), O(5)—C(5) and O(8)—C(8) are significantly shorter and C(5)—C(6) and C(8)—C(8*a*) remarkably longer than the corresponding bonds in mitomycin C (Arora, 1979).

Although there are no intramolecular hydrogen bonds, the crystal structure is built up by six intermolecular hydrogen bonds as follows: O(7)···N(1)* $(2-x, -\frac{1}{2}+y, 2-z)$, O(9*a*)···N(1) $(2-x, \frac{1}{2}+y, 2-z)$, N(1)···N(10)* $(2-x, -\frac{1}{2}+y, 2-z)$, N(1)···O(*w*) $(2-x, -\frac{1}{2}+y, 1-z)$, O(10)*···O(*w*) $(2-x, -\frac{1}{2}+y, 1-z)$ and N(10*···O(*w*) $(2-x, -\frac{1}{2}+y, 1-z)$. Thus, *A* and *B* molecules are connected to make a dimer through O(7)···N(1)* and N(1)···N(10)* hydrogen bonds, the latter involving the water molecule. *A* molecules are connected to each other through O(9*a*)···N(1) hydrogen bonds but there is no intermolecular hydrogen bond between *B* molecules.

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Structures of Colchicine Analogues. II. 2′,3′,4′-Trimethoxybiphenyl-3(and -4)-carboxylic Acid Methyl Esters

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Abstract. $C_{17}H_{18}O_5$, $M_r = 302{\cdot}3$, λ(Cu $K\alpha$) = 1·5418 Å, $T = 289$ (1) K. Methyl 2′,3′,4′-trimethoxybiphenyl-3-carboxylate (IV): monoclinic, $P2_1/c$, $a = 21{\cdot}208$ (2), $b = 5{\cdot}130$ (1), $c = 14{\cdot}172$ (2) Å, $\beta = 92{\cdot}13$ (1)°, $V = 1540{\cdot}8$ (7) Å^3, $Z = 4$, D_m(flotation) = 1·30 (1), $D_x = 1{\cdot}303$ Mg m^{-3}, $\mu = 0{\cdot}71$ mm^{-1}, $F(000) = 640$, final $R = 0{\cdot}046$ for 2282 observed data. Methyl 2′,3′,4′-trimethoxybiphenyl-4-carboxylate (V): orthorhombic, $Pna2_1$, $a = 9{\cdot}499$ (1), $b = 22{\cdot}987$ (1), $c = 14{\cdot}038$ (1) Å, $V = 3065{\cdot}2$ (3) Å^3, $Z = 8$, D_m(flotation) = 1·30 (1), $D_x = 1{\cdot}309$ Mg m^{-3}, $\mu = 0{\cdot}71$ mm^{-1}, $F(000) = 1280$, final $R = 0{\cdot}045$ for 2630 observed data. The two independent molecules of (V) adopt similar conformations with the dihedral angle

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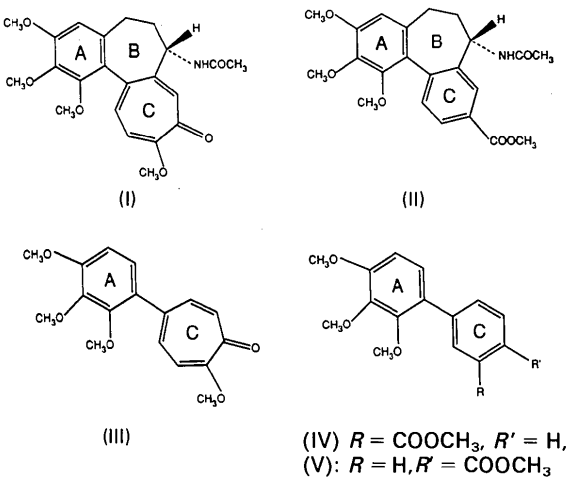
between the normals to rings *A* and *C* 59·1 (5) and 63·8 (5)° compared with 55·3 (3)° in (IV). As in colchicinoid structures with the trimethoxy substituents on ring *A*, those at C(1) and C(2) are approximately orthogonal to the ring with the methoxy at C(3) lying close to the ring plane. In (IV) the C(1) and C(2) methoxy groups point in the same direction but in (V) they point in opposite directions.

Introduction. Colchicine (I) is a potent antimitotic agent which acts by inhibition of microtubule assembly in eukaryotic cells by binding to a single high affinity site on the microtubule subunit, tubulin (Dustin, 1984). Extensive studies of the structure–activity relationships of colchicinoids have been reported in an attempt to elucidate the structural prerequisites essential for antimitotic activity (Brossi, Yeh, Chrzanowska, Wolff, Hamel, Lin, Quin, Suffness & Silverton, 1988). An important aspect of these studies has been the determination of the solid state conformations of many active analogues such as thiocolchicine (Koerntgen & Margulis, 1977), colcemid (Margulis, 1974), allocolchicine (II) (Mackay, Lacey & Burden, 1989) and colchicine itself (Lessinger & Margulis, 1978*a*), and inactive analogues such as isocolchicine (Lessinger & Margulis, 1978*b*) and colchiceine (Silverton, 1979; Mackay, Morrison & Gulbis, 1985). In an attempt to determine the minimum structural requirements for antimitotic activity, Fitzgerald (1976) synthesized the *A*/*C*-ring bicyclic analogue, 2-methoxy-5-(2′,3′,4′-trimethoxyphenyl)tropone, MTPT (III), a more potent inhibitor than colchicine, whose solid state conformation has been subsequently defined (Rossi, Link & Lee, 1984; Mackay, Sands, Lacey & Burden, 1987).*

We have extended our investigations of colchicine analogues into the more synthetically accessible bicyclic analogues of the benzoate, allocolchicine (II), to determine more fully the minimum structural requirements for activity. In the present study we report the solid state conformations of 2′,3′,4′-trimethoxybiphenyl-3-carboxylic acid methyl ester (IV) and 2′,3′,4′-trimethoxybiphenyl-4-carboxylic acid methyl ester (V). In these derivatives the structural restraint imposed by the *B* ring of allocolchicine has been eliminated, analogous to the relationship between MTPT and colchicine. Interestingly, the absence of the *B* ring reduces the microtubule inhibitory activity in the *para* ester (V) whereas the isomeric *meta* ester (IV) exhibited comparable potency to MTPT (Lacey, Burden & Watson, 1989).



Experimental. (IV) and (V) were synthesized by a modified Gomberg–Beckmann reaction of 1,2,3-trimethoxybenzene and 4-(and 3-)methoxycarbonylphenyldiazonium tetrafluoroborate according to the general procedure of Beadle, Korzeniowski, Rosenberg, Garcia-Slanga & Gokel (1984) and Lacey, Burden & Watson (1989). Colourless tabular crystals of (IV) from petroleum ether(b.p. 338–349 K)/methylene chloride; colourless prismatic crystals of (V) elongated along **a** from petroleum ether/methylene chloride mixture. Crystals *ca* 0·55 × 0·50 × 0·25 mm (IV) and 0·81 × 0·59 × 0·27 mm (V) aligned on a Rigaku-AFC diffractometer; cell parameters determined by least squares for 25 strong reflections ($38 < 2\theta < 90°$); Cu $K\alpha$ radiation (graphite-crystal monochromator, $\lambda = 1{\cdot}5418$ Å); ω–2θ scan, scan rate 4° min^{-1}, scan range ($\Delta\omega$) 1·2° + 0·5° tanθ, 10 s stationary background counts; three standard reflections monitored every 50 reflections, gradual decrease in intensity, 3·1% (IV) and 2·5% (V); intensities scaled accordingly; data to $2\theta_{max} = 130°$; 2652 unique data (h −24 to 24, k 0 to 6, l 0 to 16) of which 2282 ($I > 1{\cdot}5\sigma I$) for refinement (IV); 2721 unique data (h 0 to 11, k 0 to 27, l 0 to 16) of which 2630 ($I > \sigma I$) for refinement (V); corrections for Lorentz and polarization and for absorption [transmission factors 0·705–0·842 (IV) and 0·667–0·827 (V)]. Structures solved by direct methods with *SHELX*76 (Sheldrick, 1976); apart from methyl H atoms in (V), which were included at idealized positions, all H-atom sites located from difference syntheses and coordinates refined; full-matrix least-squares refinement with anisotropic temperature factors given to C and O atoms, isotropic for H, converged at $R = 0{\cdot}046$, $wR = 0{\cdot}072$, $S = 3{\cdot}39$ (272 parameters varied) for (IV) and $R = 0{\cdot}045$, $wR =$

* When this study was undertaken we were unaware that the atomic coordinates for MTPT determined by Rossi, Link & Lee (1984) were available. To enable comparisons with the phenylbenzoates, MTPT was prepared and X-ray coordinates obtained. Comparison of the two data sets revealed no significant differences. Our data for MTPT is thus not reported in this paper, but is noted as unpublished material in the text.

0·059, $S = 1·05$ (468 parameters varied) for (V); function minimized $\sum w(|F_o| - |F_c|)^2$ with weights $(\sigma^2|F_o| + m|F_o|^2)^{-1}$ for which m was 0·0003 and 0·003 for (IV) and (V) respectively; an isotropic extinction correction of the form $F_c = F\{1 - [2·52\,(2) \times 10^{-5}|F|^2/\sin\theta]\}$ was applied to the calculated structure amplitudes for (IV); five low-order terms (201, 002, 310, 130 and 004) apparently seriously affected by extinction were omitted from final refinement of (V). At convergence $(\Delta/\sigma)_{max} = 0·02$ (IV) [z coordinate for methyl H atom at C(3*M*)] and 0·003 (V); $(\Delta\rho)_{max}$, $(\Delta\rho)_{min} = +0·15$, $-0·17$ (IV) and $+0·19$, $-0·28$ e Å^{-3} (V). Atomic scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974). Figures prepared from the output of *ORTEP*II (Johnson, 1976). All calculations performed on a VAX11/780 computer.

Discussion. Final atomic coordinates for the non-H atoms are given in Table 1.* The molecular conformations and numbering schemes are illustrated in Fig. 1 while molecular geometry is given in Table 2.

The two independent molecules of the 4-carboxylic acid methyl ester structure, (V*a*) and (V*b*), adopt an essentially similar conformation, and the conformation of the 3′,4′-dimethoxybiphenyl moiety in the 3-carboxylic acid methyl ester (IV) is similar to that observed in (V*a*) and (V*b*). The phenyl rings in the two ester structures do not deviate significantly from planarity; the r.m.s. deviations for ring *A* atoms are 0·012 Å (IV), 0·012 Å (V*a*) and 0·008 Å (V*b*), while for ring *C* atoms the values are 0·004 Å (IV), 0·002 Å (V*a*) and 0·012 Å (V*b*). The dihedral angle between the normals to the two rings, of 55·3 (3)° in (IV), is slightly smaller than the values of 59·1 (5) and 63·8 (5)° observed in (V*a*) and (V*b*) respectively. For MTPT, in which the *B* ring is also missing, the angle between the *A* and *C* rings is 57·4° (Rossi, Link & Lee, 1984). It is interesting to note that in the colchicine structure, values of 51 and 53° were observed for this angle (Lessinger & Margulis, 1978*a*), whilst in isocolchicine the values are 53 and 57° (Lessinger & Margulis, 1978*b*). These results suggest that ring *B* has little effect on the relative orientation of rings *A* and *C*. The ester group at C(9) in (IV) and C(10) in (V) lies close to the plane of ring *C*; in (IV) it is rotated 3·3° from the plane and in (V*a*) and (V*b*) it is rotated by 2·1 and 2·3° respectively.

Table 1. *Final atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors for the non*-H *atoms with e.s.d.'s in parentheses*

	x	y	z	B_{eq}(Å^2)*
(*a*) Compound (IV)				
C(1)	3104 (1)	4766 (3)	3371 (1)	3·09 (6)
C(2)	3659 (1)	3670 (4)	3737 (1)	3·15 (5)
C(3)	3673 (1)	2470 (4)	4623 (1)	3·29 (5)
C(4)	3137 (1)	2477 (4)	5149 (2)	3·53 (6)
C(4*a*)	2594 (1)	3671 (4)	4792 (1)	3·49 (5)
C(7*a*)	1649 (1)	7842 (4)	4053 (1)	3·08 (5)
C(8)	1076 (1)	8910 (4)	3723 (1)	3·17 (5)
C(9)	804 (1)	8075 (4)	2872 (2)	3·83 (6)
C(10)	1106 (1)	6231 (5)	2346 (2)	4·45 (7)
C(12)	1673 (1)	5169 (4)	2674 (2)	4·13 (7)
C(12*a*)	1955 (1)	5957 (4)	3532 (1)	3·22 (5)
C(12*b*)	2559 (1)	4798 (4)	3899 (1)	3·20 (5)
C(13)	738 (1)	10947 (4)	4259 (1)	3·40 (6)
C(14)	770 (1)	13708 (5)	5586 (2)	4·32 (7)
C(1*M*)	3071 (2)	8473 (5)	2367 (3)	5·62 (9)
C(2*M*)	4622 (1)	5647 (6)	3406 (2)	5·07 (9)
C(3*M*)	4239 (1)	−234 (6)	5727 (2)	5·17 (8)
O(1)	3102 (1)	5717 (3)	2462 (1)	4·07 (4)
O(2)	4188 (1)	3594 (3)	3195 (1)	4·03 (4)
O(3)	4236 (1)	1359 (3)	4902 (1)	4·22 (4)
O(4)	237 (1)	11864 (3)	4014 (1)	5·25 (5)
O(5)	1057 (1)	11673 (3)	5047 (1)	3·75 (4)
(*b*) Compound (V): molecule (V*a*) – atoms 1 to 14; molecule (V*b*) – atoms 21 to 34				
C(1)	6321 (2)	2836 (1)	1544	3·05 (7)
C(2)	6286 (3)	3442 (1)	1453 (3)	3·10 (7)
C(3)	6143 (3)	3791 (1)	2266 (3)	3·29 (7)
C(4)	5967 (3)	3537 (1)	3149 (3)	3·55 (8)
C(4*a*)	5953 (3)	2932 (1)	3223 (3)	3·43 (7)
C(7*a*)	5009 (3)	1660 (1)	2986 (3)	4·01 (9)
C(8)	5013 (3)	1058 (1)	3153 (3)	3·97 (8)
C(9)	6181 (3)	733 (1)	2907 (3)	3·22 (7)
C(10)	7342 (3)	1003 (1)	2489 (3)	3·34 (7)
C(12)	7323 (3)	1598 (1)	2325 (3)	3·29 (7)
C(12*a*)	6150 (3)	1933 (1)	2570 (3)	3·03 (7)
C(12*b*)	6148 (2)	2575 (1)	2439 (3)	3·04 (7)
C(13)	6146 (3)	91 (1)	3093 (3)	3·65 (8)
C(14)	7463 (4)	−785 (1)	3096 (4)	5·16 (11)
C(1*M*)	7672 (4)	2570 (2)	183 (4)	5·42 (11)
C(2*M*)	5056 (3)	3871 (2)	188 (3)	4·85 (10)
C(3*M*)	6044 (4)	4756 (1)	2899 (3)	5·01 (11)
O(1)	6431 (2)	2492 (1)	755 (3)	4·05 (6)
O(2)	6392 (2)	3698 (1)	567 (3)	3·83 (6)
O(3)	6148 (2)	4375 (1)	2096 (3)	4·34 (7)
O(4)	5140 (3)	−163 (1)	3396 (3)	5·68 (9)
O(5)	7378 (2)	−165 (1)	2900 (3)	4·41 (7)
C(21)	1389 (2)	7827 (1)	1799 (3)	2·82 (7)
C(22)	1420 (2)	8437 (1)	1823 (3)	2·81 (7)
C(23)	1603 (3)	8753 (1)	980 (3)	2·99 (7)
C(24)	1791 (3)	8464 (1)	128 (3)	3·24 (7)
C(24*a*)	1798 (3)	7855 (1)	120 (3)	3·16 (8)
C(27*a*)	2785 (3)	6573 (1)	644 (3)	3·44 (7)
C(28)	2742 (3)	5974 (1)	539 (3)	3·42 (7)
C(29)	1494 (3)	5669 (1)	666 (3)	3·00 (7)
C(30)	295 (3)	5970 (1)	942 (3)	3·813 (7)
C(32)	339 (3)	6572 (1)	1051 (3)	3·77 (8)
C(32*a*)	1566 (3)	6881 (1)	889 (3)	2·92 (7)
C(32*b*)	1597 (3)	7534 (1)	935 (3)	2·89 (7)
C(33)	1494 (3)	5031 (1)	490 (3)	3·46 (8)
C(34)	76 (4)	4179 (1)	496 (3)	4·83 (10)
C(21*M*)	−81 (3)	7574 (2)	3096 (3)	5·05 (11)
C(22*M*)	2535 (3)	8845 (1)	3147 (3)	4·50 (10)
C(23*M*)	1803 (4)	9694 (1)	271 (3)	4·33 (9)
O(21)	1257 (2)	7514 (1)	2623 (3)	3·66 (6)
O(22)	1246 (2)	8726 (1)	2674 (2)	3·45 (5)
O(23)	1613 (2)	9341 (1)	1091 (2)	3·80 (6)
O(24)	2467 (2)	4764 (1)	172 (3)	4·83 (7)
O(25)	248 (2)	4790 (1)	709 (3)	4·19 (7)

*$B_{eq} = \frac{8}{3}\pi^2\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

Superimposition of the trimethoxy rings (Fig. 2) illustrates that the *C*-ring regions of allocolchicine and the *para*-biphenyl ester (V) overlap. In contrast, the ester function of the more active *meta*-biphenyl ester (IV) is displaced from the ester groups of (II)

* Lists of structure amplitudes, anisotropic thermal parameters, H-atom coordinates and short intermolecular approaches have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52003 (58 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

and (V). In the solid state, the methyl carboxylate group of (IV) and the tropolone methoxy of MTPT (Rossi *et al.*, 1984) lie on the opposite side of the *C*-ring methoxyl of colchicine with respect to the *A*-ring methoxy substituents. However, in solution, the free rotation about the *A*/*C*-ring axis in MTPT (Rossi *et al.*, 1984) and therefore (IV) would lead to a closer proximity of both the methoxy groups of MTPT and (IV) to the methoxyl of the *C* ring in colchicine (Fig. 2). The comparable activity of (III) and (IV) suggests that interaction of the *C* ring with the receptor is closer to a *meta* than to a *para* substitution. These observations support the argument that the role of the *B* ring in colchicinoids relates to the maintenance of the *A*/*C*-ring conformation.

As in the other solid state structures of colchicinoids which contain the three methoxy substituents of the *A* ring, those at C(1) and C(2) are roughly perpendicular to the ring plane whereas the substituent at C(3) lies close to the plane [see torsion angles C(2)—C(1)—O(1)—C(1*M*), C(3)—C(2)—O(2)—C(2*M*) and C(4)—C(3)—O(3)—C(3*M*) in Table 2]. In (IV), as in colchicine, thiocolchicine (Koerntgen & Margulis, 1977) and the 2-methoxy-5-(2′,3′,4′-trimethoxyphenyl)tropone, the methoxy groups at C(1) and C(2) point in the same direction. This is not so in the structure of (V) in which these methoxy substituents point in opposite directions as observed in crystals of colchiceine (Silverton, 1979; Mackay, Morrison & Gulbis, 1985). In crystals of isocolchicine and *N*-acetyldemecoline (Silverton, Sharma & Brossi, 1985) both of these orientations are observed, whereas in crystals of colchiceine acetate (Miravitlles, Solans, Bladé-Font, Germain & Declercq, 1982) and colchiceine benzoate (Molins, Rius, Solans, Miravitlles, Bladé-Font & Germain,

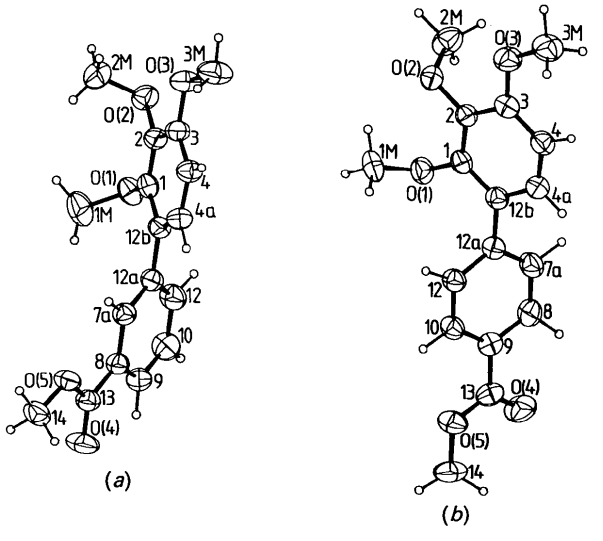


Fig. 1. Perspective views of (*a*) *meta*-biphenyl ester (IV) and (*b*) *para*-biphenyl ester (V). The C symbol is omitted for carbons and the H atoms are denoted by spheres of arbitrary radius. Thermal ellipsoids indicate 50% probability.

Table 2. *Bond lengths* (Å), *valence angles* (°) *and selected torsion angles* (°) *with e.s.d.'s in parentheses*

	(IV)	(V*a*)	(V*b*)		
C(1)—C(2)	1·388 (3)	1·399 (3)	1·403 (3)		
C(1)—C(12*b*)	1·401 (3)	1·402 (4)	1·401 (5)		
C(1)—O(1)	1·377 (2)	1·365 (4)	1·368 (5)		
C(2)—C(3)	1·398 (3)	1·402 (5)	1·399 (5)		
C(2)—O(2)	1·384 (3)	1·380 (6)	1·377 (5)		
C(3)—C(4)	1·382 (3)	1·380 (6)	1·380 (5)		
C(3)—O(3)	1·368 (3)	1·363 (3)	1·361 (3)		
C(4)—C(4*a*)	1·383 (3)	1·395 (3)	1·400 (3)		
C(4*a*)—C(12*b*)	1·390 (3)	1·385 (5)	1·375 (5)		
C(7*a*)—C(8)	1·397 (3)	1·404 (3)	1·385 (3)		
C(7*a*)—C(12*a*)	1·392 (3)	1·382 (4)	1·400 (4)		
C(8)—C(9)	1·387 (3)	1·381 (4)	1·389 (4)		
C(8)—C(13)	1·490 (3)				
C(9)—C(10)	1·377 (3)	1·395 (4)	1·387 (4)		
C(9)—C(13)		1·499 (3)	1·487 (3)		
C(10)—C(12)	1·385 (3)	1·387 (3)	1·393 (3)		
C(12)—C(12*a*)	1·395 (3)	1·397 (4)	1·384 (4)		
C(12*a*)—C(12*b*)	1·489 (3)	1·487 (3)	1·503 (3)		
C(13)—O(4)	1·201 (3)	1·198 (4)	1·196 (4)		
C(13)—O(5)	1·337 (3)	1·338 (4)	1·342 (4)		
C(14)—O(5)	1·442 (3)	1·454 (3)	1·445 (3)		
C(1*M*)—O(1)	1·422 (3)	1·438 (5)	1·441 (4)		
C(2*M*)—O(2)	1·423 (4)	1·432 (4)	1·419 (4)		
C(3*M*)—O(3)	1·426 (3)	1·431 (5)	1·420 (5)		
C(2)—C(1)—C(12*b*)	120·7 (1)	120·3 (2)	119·9 (2)		
C(2)—C(1)—O(1)	117·8 (1)	120·3 (2)	120·5 (2)		
C(12*b*)—C(1)—O(1)	121·5 (1)	119·2 (2)	119·5 (2)		
C(1)—C(2)—C(3)	120·2 (1)	119·9 (2)	120·1 (2)		
C(1)—C(2)—O(2)	119·9 (1)	120·3 (2)	120·0 (2)		
C(3)—C(2)—O(2)	119·7 (2)	119·8 (2)	119·9 (2)		
C(2)—C(3)—C(4)	119·5 (2)	120·1 (2)	120·0 (2)		
C(2)—C(3)—O(3)	115·6 (1)	114·9 (2)	114·8 (2)		
C(4)—C(3)—O(3)	124·9 (2)	125·0 (2)	125·2 (2)		
C(3)—C(4)—C(4*a*)	119·6 (2)	119·3 (2)	119·3 (2)		
C(4)—C(4*a*)—C(12*b*)	122·2 (2)	122·0 (2)	122·0 (2)		
C(8)—C(7*a*)—C(12*a*)	120·8 (2)	121·1 (2)	120·3 (2)		
C(7*a*)—C(8)—C(9)	119·9 (2)	119·6 (2)	120·9 (2)		
C(7*a*)—C(8)—C(13)	122·3 (2)				
C(9)—C(8)—C(13)	117·9 (2)				
C(8)—C(9)—C(10)	119·8 (2)	120·0 (2)	119·0 (2)		
C(8)—C(9)—C(13)		118·1 (2)	118·4 (2)		
C(10)—C(9)—C(13)		121·9 (2)	122·6 (2)		
C(9)—C(10)—C(12)	120·3 (2)	119·9 (2)	120·1 (2)		
C(10)—C(12)—C(12*a*)	121·2 (2)	120·9 (2)	121·1 (2)		
C(7*a*)—C(12*a*)—C(12)	118·1 (2)	118·6 (2)	118·5 (2)		
C(7*a*)—C(12*a*)—C(12*b*)	120·2 (2)	120·1 (2)	120·0 (2)		
C(12)—C(12*a*)—C(12*b*)	121·7 (1)	121·2 (2)	121·5 (2)		
C(1)—C(12*b*)—C(4*a*)	117·7 (1)	118·3 (2)	118·8 (2)		
C(1)—C(12*b*)—C(12*a*)	122·2 (1)	122·4 (2)	121·0 (2)		
C(4*a*)—C(12*b*)—C(12*a*)	120·1 (1)	119·3 (2)	120·2 (2)		
C(9)—C(13)—O(4)		124·0 (2)	124·6 (2)		
C(9)—C(13)—O(5)		112·2 (2)	111·6 (2)		
C(8)—C(13)—O(4)	124·4 (2)				
C(8)—C(13)—O(5)	112·5 (2)				
O(4)—C(13)—O(5)	123·1 (1)	123·7 (2)	123·7 (2)		
C(1)—O(1)—C1*M*)	116·1 (2)	116·3 (2)	114·9 (2)		
C(2)—O(2)—C(2*M*)	113·2 (2)	112·9 (2)	113·3 (2)		
C(3)—O(3)—C(3*M*)	116·9 (2)	117·7 (2)	118·4 (2)		
C(13)—O(5)—C(14)	115·7 (2)	116·2 (2)	117·0 (2)		
				(I)	
C(2)—C(1)—O(1)—C(1*M*)	−109·8 (2)	60·6 (4)	67·3 (4)	−79	−94
C(3)—C(2)—O(2)—C(2*M*)	−86·4 (2)	−80·2 (4)	−89·4 (3)	−68	−76
C(4)—C(3)—O(3)—C(3*M*)	9·9 (3)	3·8 (5)	1·4 (5)	14	−4
C(1)—C(12*b*)—C(12*a*)—C(7*a*)	−126·4 (2)	−122·9 (3)	−115·1 (4)	54	52
C(12)—C(12*a*)—C(12*b*)—C(1)	54·9 (3)	60·6 (4)	67·2 (4)	53	53
C(7*a*)—C(8)—C(13)—O(4)	−177·9 (2)				
C(7*a*)—C(8)—C(13)—O(5)	2·6 (3)				
C(8)—C(13)—O(5)—C(14)	177·9 (2)				
O(4)—C(13)—O(5)—C(14)	−1·7 (3)	−1·2 (3)	−3·3 (5)		
C(9)—C(13)—O(5)—C(14)		177·6 (3)	175·2 (3)		
C(10)—C(9)—C(13)—O(4)		−175·3 (3)	173·0 (3)		
C(10)—C(9)—C(13)—O(5)		6·0 (4)	−5·4 (4)		

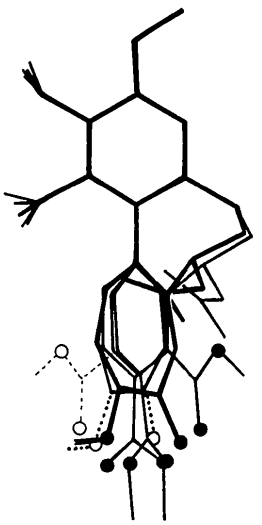


Fig. 2. The molecular skeletons of colchicine, allocolchicine, MTPT, *meta*-biphenyl ester (IV) and *para*-biphenyl ester (V) with their *A* rings superimposed. For comparison of the relative positions of the *C*-ring methoxy groups, the *C* rings of MTPT (dotted lines) and (IV) also (broken lines) have been rotated 180° around their *A*/*C*-ring axes. Oxygens of the *C*-ring substituents are denoted by spheres.

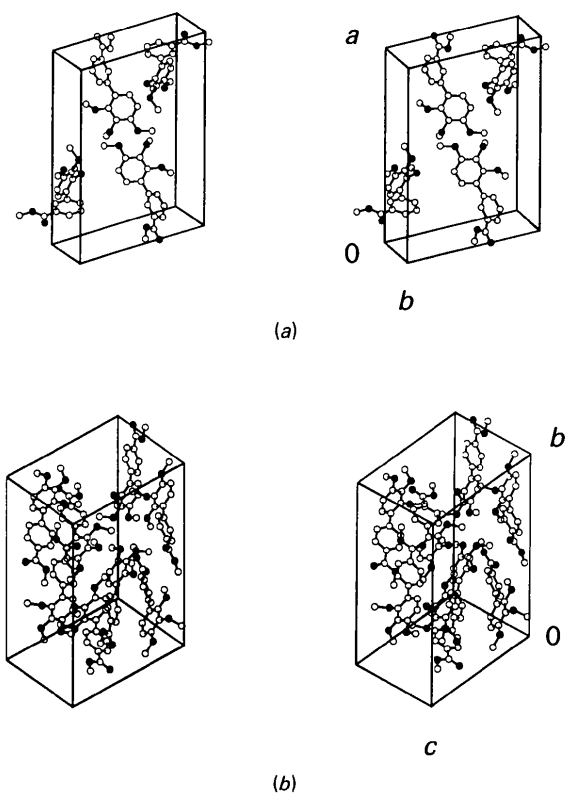


Fig. 3. Stereoviews of the crystal packings of (*a*) *meta*-biphenyl ester (IV) and (*b*) *para*-biphenyl ester (V).

1985), although the C(2) and C(3) methoxy groups point in the same direction, they are pointing in the opposite direction relative to (IV), colchicine, thiocolchicine and the tropone structure mentioned above. The different orientations of these methoxy groups in these colchicine analogues is most likely a consequence of the different packing modes in the crystals.

The crystal packing of (IV) and (V) is illustrated in Fig. 3. As only hydrogen-bond acceptors are present in the molecules and the crystals are not solvated, hydrogen-bond formation is precluded. Consequently, the molecules are held together by van der Waals interactions. The shortest intermolecular contacts are O(4)···C(14) $(-x, 3-y, 1-z)$ 3·183 (3) Å in (IV) and C(2*M*)···O(24) 3·203 (4), O(4)···O(25) $(\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}+z)$ 3·270 (6), O(3)···O(23) $(\frac{1}{2}+x, \frac{3}{2}-y, z)$ 3·301 (4), O(4)···C(34) $(\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}+z)$ 3·320 (6) and C(3*M*)···O(23) $(\frac{1}{2}+x, \frac{3}{2}-y, z)$ 3·323 (4) Å in (V). The molecules are present in the structures as mirror image conformers.

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