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Structure and Conformation of 2-Methyl-2-(2-naphthyloxy)-4*H*-1,3-benzodioxin-4-one

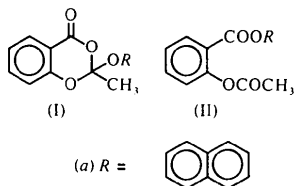
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Abstract. C₁₉H₁₄O₄, monoclinic, $P2_1/c$, $a = 15.32$ (2), $b = 7.59$ (1), $c = 13.16$ (2) Å, $\beta = 80.7$ (8)°, $Z = 4$, $U = 1509$ Å³, $D_c = 1.35$ Mg m⁻³, $\mu = 0.1079$ mm⁻¹, $R = 0.068$ for 1204 reflexions [$I > 3\sigma(I)$] and 236 parameters. The β -naphthyloxy group is axial to the B ring which has an envelope conformation.

Introduction. The synthesis of the title compound (Ia) was first reported by Rüchardt & Rochlitz (1974). It has been prepared in this laboratory together with ten other cyclic *ortho* esters of the type 2-substituent-2-methyl-4*H*-1,3-benzodioxin-4-one (I) in a search for acetylsalicylic acid (aspirin) prodrugs (Hansen & Senning, 1981). Analogous compounds with the 1,3-benzodioxin moiety as part of a triglyceride structure have been prepared and tested for anti-inflammatory activity recently (Paris, Garmaise, Cimon, Swett, Carter & Young, 1980).



Compounds of type (I) are cyclic isomers of normal esters of acetylsalicylic acid (II). They are formed *via* an intermediate 2-methyl-4-oxo-4*H*-1,3-benzodioxin-2-ylum ion in a kinetically controlled reaction between acetylsalicyloyl chloride and alcohols/phenols. However, this acid chloride shows ambivalent reactivity and, depending on reaction conditions, varying amounts of the normal esters of type (II) are also

formed. The reaction of acetylsalicyloyl chloride with β -naphthol (in acetonitrile at 253 K) yielded (Ia) as the main product. By repeated recrystallization from petroleum ether (b.p. 313–323 K) and subsequent drying *in vacuo*, transparent, pale-yellow single crystals (m.p. 361.7–362.7 K) were obtained for X-ray analysis.

X-ray structure analysis was carried out to ascertain the cyclic structure of (Ia) and to confirm the interpretation of spectroscopic data for type (I) compounds. Prior to the X-ray investigation reported here, the cyclic structure of type (I) compounds had been deduced solely from spectroscopic data (Rüchardt & Rochlitz, 1974; Hansen & Senning, 1981). Knowledge of the conformation is also of importance for the interpretation of the hydrolysis data of compounds of type (I) (Hansen & Senning, 1981). Furthermore, this is, to our knowledge, the first X-ray structure analysis of this type of cyclic *ortho* ester.

The crystal used for the structure determination was grown from a petroleum ether solution and had approximate dimensions 0.80 × 0.55 × 0.35 mm. The space group $P2_1/c$ was determined from the systematic absences on precession pictures of the (0*kl*) and (*h*0*l*) layers. Weissenberg pictures of zero and first-layer lines showed spots with tails, indicating a large mosaic spread. Cell dimensions were calculated from the setting angles of 14 reflexions measured on a Picker FACS-1 diffractometer using Mo $K\alpha$ radiation.

The data were collected on a Buerger automated X-ray diffractometer from Charles Supper Company, Inc., using Mo $K\alpha$ radiation. The crystal was mounted with the b axis as rotation axis. Reflexions with $k = 0$ and $k = 1$ were measured out to $\sin \theta = 0.50$. Other reflexions were measured out to $\sin \theta = 0.45$. 3155 independent reflexions were measured, and back-

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ground–peak–background scans were used. Stability was checked by measuring global standards between each layer and local standards within each layer. A slight decrease in intensity of the global standards during the data collection was corrected for. During the data reduction correction was made for Lp effects and symmetry-related reflexions were averaged. No absorption or extinction corrections were made.

The structure was solved with *MULTAN 77* (Main, Lessinger, Woolfson, Germain & Declercq, 1977). The 23 highest peaks in the *E* map were interpreted as being the positions of the non-H atoms. Of the eight solutions proposed by *MULTAN*, that chosen had the best ABSFOM and RESID.

The positions of the H atoms were found where expected in a difference Fourier synthesis after refinement of positional and anisotropic thermal parameters for C and O atoms. Least-squares refinement of a scale factor, atomic coordinates, anisotropic temperature factor parameters for the non-H atoms and isotropic for the H atoms gave $R = 0.068$ for 1204 reflexions with $I > 3\sigma(I)$ and 236 parameters. The least-squares refinement was carried out in two steps, seven H atoms being kept fixed in each, and unit weights were used.

Scattering factors were taken from Cromer & Mann (1968) for C and O and from Stewart, Davidson & Simpson (1965) for H. The following programs were used: data reduction: *DSORTH*, difference Fourier: *JIMDAP*, least-squares refinement: *LINEX* (State University of New York, Buffalo), distances and angles: *ORFFE* (Busing, Martin & Levy, 1964), drawing: *ORTEP* (Johnson, 1965).

Discussion. Atomic coordinates and bond angles are given in Tables 1 and 2.* Bond lengths are shown in Fig. 1. The C–H bond lengths were found in the range 0.76–1.12 Å (e.s.d.'s 0.05–0.08 Å). The *B* ring is the most interesting part of the molecule and from Fig. 1 and Table 3 it is seen to have an envelope conformation with O(1) and O(2) almost in the plane of the benzene (*A*) ring. The exocyclic β -naphthyloxy group is axial to the *B* ring and, though it has not been proved, this conformation is believed to exist in the other compounds of type (I). $^1\text{H-NMR}$ and IR spectroscopy had formerly indicated a cyclic structure of that kind for the series of compounds of type (I) (Rüchardt & Rochlitz, 1974). Further evidence for the assigned cyclic structure was obtained from $^{13}\text{C-NMR}$ and UV spectroscopy (Hansen & Senning, 1981), and from $^{13}\text{C-NMR}$ of analogous compounds (Paris *et al.*, 1980). These features also applied to (Ia) and the inter-

pretation of the spectroscopic data is thus confirmed by the X-ray analysis.

Table 1. *Fractional atomic coordinates* ($\times 10^4$ for C and O, $\times 10^3$ for H) and *isotropic thermal parameters* ($\times 10^3$ for C and O, $\times 10^2$ for H)

$$U_{\text{iso}} = \frac{1}{3} \sum_i \sum_j a_i^* a_j^* a_{ij}$$

	<i>x</i>	<i>y</i>	<i>z</i>	U_{iso} (Å ²)
C(1)	3705 (4)	2837 (9)	8497 (7)	57 (3)
C(2)	3742 (3)	2414 (9)	7463 (7)	56 (4)
C(3)	4017 (3)	775 (9)	7055 (6)	63 (3)
C(4)	4250 (4)	−442 (11)	7753 (8)	70 (4)
C(5)	4236 (5)	−46 (11)	8774 (9)	76 (4)
C(6)	3969 (5)	1593 (13)	9154 (8)	72 (4)
C(7)	3465 (4)	4639 (10)	8839 (8)	71 (4)
C(8)	2927 (4)	4952 (8)	7242 (6)	63 (3)
C(9)	2909 (4)	6395 (9)	6448 (6)	73 (3)
C(10)	699 (5)	4360 (9)	7186 (7)	65 (3)
C(11)	1540 (4)	3786 (8)	6952 (6)	55 (3)
C(12)	1792 (4)	2698 (9)	6070 (6)	60 (3)
C(13)	1183 (4)	2261 (9)	5467 (6)	67 (3)
C(14)	−353 (5)	2332 (11)	5143 (7)	67 (3)
C(15)	−1212 (5)	2837 (10)	5412 (8)	86 (4)
C(16)	−1463 (5)	3895 (11)	6259 (8)	80 (4)
C(17)	−852 (4)	4436 (9)	6849 (7)	70 (3)
C(18)	42 (4)	3901 (8)	6589 (6)	56 (3)
C(19)	304 (4)	2822 (8)	5714 (6)	61 (3)
O(1)	3543 (2)	3653 (6)	6766 (3)	53 (2)
O(2)	3224 (3)	5725 (6)	8103 (4)	68 (2)
O(3)	3537 (4)	5240 (7)	9669 (5)	94 (3)
O(4)	2122 (2)	4201 (5)	7632 (4)	58 (2)
H(3)	394 (6)	58 (15)	651 (8)	17 (6)
H(4)	446 (4)	−158 (10)	748 (6)	11 (3)
H(5)	430 (3)	−88 (7)	929 (5)	5 (2)
H(6)	377 (4)	334 (10)	469 (5)	7 (3)
H(10)	55 (3)	2 (6)	267 (4)	1 (1)
H(12)	233 (3)	280 (6)	99 (4)	4 (2)
H(13)	137 (4)	151 (9)	493 (5)	8 (2)
H(14)	25 (3)	−324 (6)	44 (4)	2 (2)
H(15)	−165 (5)	241 (10)	500 (6)	11 (3)
H(16)	−210 (4)	441 (8)	639 (5)	8 (2)
H(17)	−98 (4)	516 (8)	752 (5)	7 (2)
H(91)	240 (5)	−229 (11)	188 (6)	12 (3)
H(92)	262 (3)	−103 (7)	98 (4)	4 (2)
H(93)	346 (4)	−179 (8)	129 (5)	8 (2)

Table 2. *Bond angles* (°) for the non-H atoms

C(2)–C(1)–C(6)	119.0 (8)	C(10)–C(11)–C(12)	119.8 (8)
C(2)–C(1)–C(7)	119.0 (8)	O(4)–C(11)–C(12)	122.3 (6)
C(1)–C(2)–O(1)	121.0 (7)	C(13)–C(12)–C(11)	119.7 (6)
C(2)–C(3)–C(4)	115.7 (9)	C(12)–C(13)–C(19)	121.0 (7)
C(5)–C(4)–C(3)	122.4 (9)	C(15)–C(14)–C(19)	122.3 (9)
C(6)–C(5)–C(4)	121 (1)	C(16)–C(15)–C(14)	120.4 (9)
C(5)–C(6)–C(1)	119 (1)	C(15)–C(16)–C(17)	120.4 (8)
O(3)–C(7)–O(2)	119.3 (9)	C(16)–C(17)–C(18)	119.9 (9)
O(4)–C(8)–O(1)	111.3 (5)	C(19)–C(18)–C(17)	119.9 (9)
O(4)–C(8)–C(9)	116.1 (6)	C(19)–C(18)–C(10)	117.4 (7)
O(1)–C(8)–C(9)	106.2 (7)	C(17)–C(18)–C(10)	122.7 (8)
O(4)–C(8)–O(2)	104.9 (4)	C(18)–C(19)–C(14)	117.1 (7)
O(2)–C(8)–O(1)	111.1 (6)	C(18)–C(19)–C(13)	120.0 (7)
O(2)–C(8)–C(9)	107.2 (6)	C(14)–C(19)–C(13)	122.9 (8)
O(2)–C(7)–C(1)	115.3 (9)	C(2)–O(1)–C(8)	112.2 (6)
C(11)–C(10)–C(18)	122.1 (8)	C(7)–O(2)–C(8)	118.4 (6)
C(10)–C(11)–O(4)	117.8 (7)	C(8)–O(4)–C(11)	118.7 (6)

* Lists of structure factors, anisotropic thermal parameters and C–H bond lengths have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36439 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

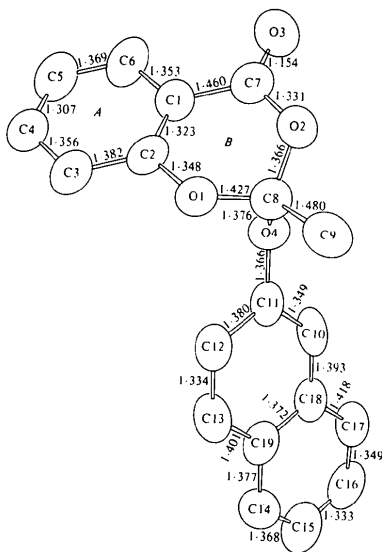


Fig. 1. ORTEP diagram of (Ia) and bond lengths (Å) (e.s.d.'s 0.008–0.010 Å). The thermal motion ellipsoids are set at the 50% level. H atoms are not shown.

Table 3. Distances (Å) from (a) naphthalene plane, (b) benzene plane

(a)	(b)
C(10) 0.061 (8)	C(1) -0.011 (6)
C(11) 0.034 (7)	C(2) 0.003 (6)
C(12) 0.007 (7)	C(3) 0.008 (6)
C(13) 0.020 (8)	C(4) -0.011 (7)
C(14) -0.029 (9)	C(5) 0.002 (8)
C(15) -0.074 (8)	C(6) 0.009 (9)
C(16) -0.041 (8)	C(7) 0.077 (7)
C(17) 0.021 (8)	C(8) -0.503 (7)
C(18) 0.047 (7)	O(1) 0.075 (4)
C(19) 0.022 (7)	O(2) 0.054 (5)
O(4) -0.051 (5)	O(3) 0.275 (6)

Theoretically, compound (Ia) could be formed with the exocyclic group both in the axial and the equatorial position or in either of them. However, only in the

observed axial position is the C(8)–O(4) bond anti-periplanar to the electron pairs of O(1) and O(2), and the specific formation of (Ia) seems to constitute an example of *ortho* ester formation with stereoelectronic control (Deslongchamps, 1977). Recently, stereoelectronic effects were also observed to control the specific formation of some *cis* tricyclic acetals *via* intermediate oxenium ions (Beaulieu, Dickinson & Deslongchamps, 1980). The specific formation of (Ia) *via* an intermediate 1,3-benzodioxenium ion is analogous to that, and the observed conformation is thus believed to be controlled by stereoelectronic effects.

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