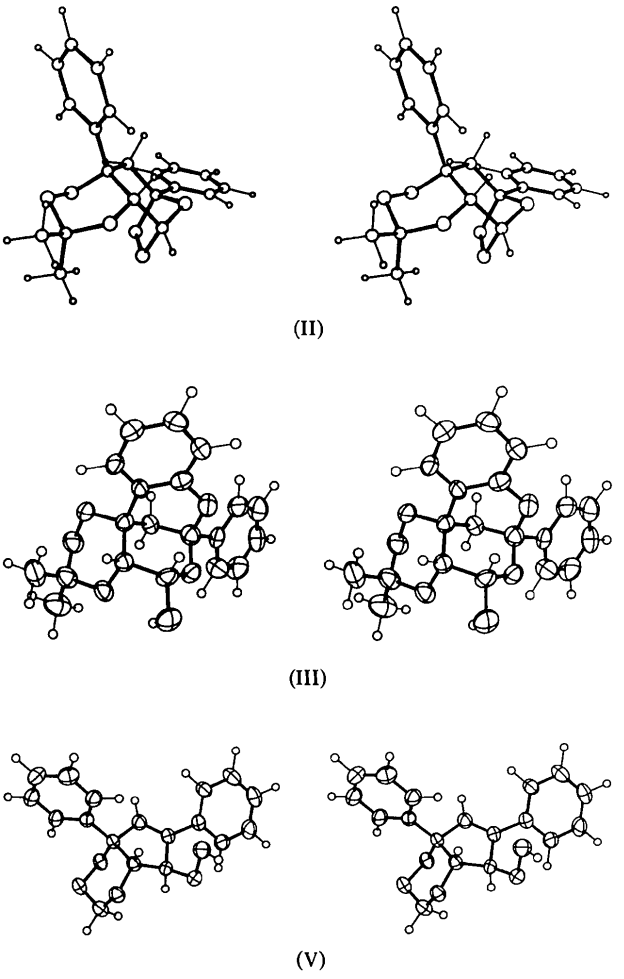

Fig. 1. Stereoviews of 1,2,4-trioxane derivatives: (II) ozonide, (III) spirocyclic acetal and (V) hydroperoxide.

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References

ALLEN, F. H., BELLARD, S., BRICE, M. D., CARTWRIGHT, B. A., DOUBLEDAY, A., HIGGS, H., HUMMELINK, T., HUMMELINK-PETERS, B. G., KENNARD, O., MOTHERWELL, W. D. S., RODGERS, J. R. & WATSON, D. G. (1979). *Acta Cryst.* B**35**, 2331–2339.

ALLEN, F. H., BELLARD, S. A. & KENNARD, O. (1986). *Acta Cryst.* C**42**, 829–832.

BROWN, I. D. (1985). *Acta Cryst.* A**41**, 339.

CREMER, D. & POPLE, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JEFFORD, C. W., BOUKOUVALAS, J., JAGGI, D., KOHMOTO, S. & BERNARDINELLI, G. (1986). *Helv. Chim. Acta*, **69**, 941–948.

JEFFORD, C. W., BOUKOUVALAS, J., KOHMOTO, S. & BERNARDINELLI, G. (1985). *Tetrahedron*, **41**, 2081–2088.

JEFFORD, C. W., FERRO, S., MOULIN, M.-C., VELARDE, J., JAGGI, D., KOHMOTO, S., RICHARDSON, G. D., GODOY, J., ROSSIER, J.-C., BERNARDINELLI, G. & BOUKOUVALAS, J. (1986). *New Trends Nat. Prod. Chem.* **26**, 163–183. Elsevier. In the press.

JEFFORD, C. W., JAGGI, D., BOUKOUVALAS, J., KOHMOTO, S. & BERNARDINELLI, G. (1984*a*). *Helv. Chim. Acta*, **67**, 1104–1111.

JEFFORD, C. W., JAGGI, D., BOUKOUVALAS, J., KOHMOTO, S. & BERNARDINELLI, G. (1984*b*). *Helv. Chim. Acta*, **67**, 2254–2260.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

NARDELLI, M. (1983). *Acta Cryst.* C**39**, 1141–1142.

QINGHAOSU ANTIMALARIAL COORDINATING RESEARCH GROUP (1979). *Chin. Med. J.* **92**, 811–819.

STEWART, J. M., MACHIN, P. A., DICKINSON, C. W., AMMON, H. L., HECK, H. & FLACK, H. (1976). The *XRAY*76 system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.

WILSON, R. M., GARDNER, E. J., ELDER, R. C., SQUIRE, R. H. & FLORIAN, L. R. (1974). *J. Am. Chem. Soc.* **96**, 2955–2963.

YAMAMOTO, H., AOYAMA, H., OMOTE, Y., AKUTAGAWA, M., TAKENAKA, A. & SASADA, Y. (1977). *J. Chem. Soc. Chem. Commun.* pp. 63–64.

YAMAMOTO, H., NAKAI, I., KASHIMA, C., OMOTE, Y. & AKUTAGAWA, M. (1983). *Chem. Lett.* pp. 1841–1844.

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Structure of Erythrosine B Ethanolate

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Abstract. $C_{20}H_8I_4O_5.C_2H_6O$, $M_r = 881{\cdot}95$, monoclinic, $P2_1/n$, $a = 12{\cdot}509\ (3)$, $b = 12{\cdot}940\ (2)$, $c = 16{\cdot}129\ (3)$ Å, $\beta = 111{\cdot}6\ (1)°$, $V = 2427{\cdot}4\ (2)$ Å^3, $Z = 4$, $D_x = 2{\cdot}41$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71069$ Å, $\mu = 51{\cdot}14$ cm^{-1}, $F(000) = 1624$, $T = 295$ K, $R = 0{\cdot}071$ for 6065 unique reflections. Erythrosine B, also known as FD and C Red No. 3, crystallizes as a free acid–ethanol solvate. The relative orientation of the benzoic acid and

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xanthene moieties is nearly perpendicular. There are short I···I and I···O contact distances in the crystal structure of this iodothyronine deiodinase enzyme inhibitor, as observed in thyroid hormone structures.

Introduction. Erythrosine B, tetraiodofluorescein {3′,6′-dihydroxy-2′,4′,5′,7′-tetraiodospiro[isobenzofuran-1(3*H*),9′-[9*H*]xanthen]-3-one disodium salt}, is a red dye widely used as a biological stain and is certified by the Food and Drug Administration as a color additive in food and drugs.

Anionic xanthene dyes have been shown to exert a wide range of pharmacological effects in excitable tissues. For example, erythrosine B has been shown to influence acetylcholine release, inhibit Na–K ATPase activity and cardiac glycoside binding, as well as inhibit thyroid function (Levitan, 1977; Smith, Dombro & Zidichouski, 1984; Vought, Brown & Wolff, 1972; Ruiz & Ingbar, 1982). Since the general population ingests large quantities of erythrosine B as a red food coloring and because of its high iodine content its effects on thyroid function are of importance. It has been shown that erythrosine B decreases serum protein-bound iodine levels and decreases 24 h iodine uptakes (Vought, Brown & Wolff, 1972). Recent studies show that erythrosine B and Rose Bengal, its polychlorophenyl derivative, inhibit thyroxine deiodination (Mol, Docter, Hennemann & Visser, 1982), whereas fluorescein, the nonhalogenated parent compound, has no activity in the deiodinase enzyme system (Fekkes, Hennemann & Visser, 1982).

Because of the structural homologies between erythrosine B and the thyroid hormones, its crystal structure was investigated and its conformation compared with the thyroid hormones (Cody, 1985).

Experimental. Red crystals of erythrosine B (Sigma, St Louis) were grown from ethanol (90%) at room temperature; cell dimensions from least-squares refinement of 25 reflections, 2θ range 25·42–32·78°; Nicolet *P*3 diffractometer, Nb-filtered Mo $K\alpha$ radiation, θ–2θ scan, $2\theta_{max} = 60°$, $0 \le h \le 18$, $0 \le k \le 19$, $-22 \le l \le 23$; 0·12 × 0·30 × 0·40 mm; four standard reflections monitored every 96 reflections, no crystal decomposition, Lp correction applied but no corrections for extinction or absorption, $\mu = 51{\cdot}14\ cm^{-1}$, 7146 unique reflections, 6065 with $I > 3\sigma(I)$ (Stout & Jensen, 1968); direct methods (*MULTAN*: Germain, Main & Woolfson, 1971; *NQEST*: DeTitta, Edmonds, Langs & Hauptman, 1975), refinement on *F* by full-matrix least squares, anisotropic thermal parameters, H positions assigned and held fixed; final difference Fourier maps showed no peaks $> 0{\cdot}2\ e\ Å^{-3}$, $\sum w(|F_o - F_c|)^2$ minimized, $w = 1/[\sigma^2(I) + (0{\cdot}02I)^2]$, final $R = 0{\cdot}071$, $wR = 0{\cdot}068$ for 6065 reflections, max. $\Delta/\sigma = -0{\cdot}01$; atomic scattering factors from *International Tables for X-ray Crystallography* (1974); all calculations performed on a VAX 11/780 computer using Enraf–Nonius (1979) *SDP*.

Discussion. Final fractional coordinates and equivalent *B* values for erythrosine B ethanolate are listed in Table 1.* Fig. 1 shows the atom-labeling scheme and the molecular conformation of erthyrosine B which shows that the relative orientation of the benzoic acid and xanthene moieties are nearly perpendicular. The dihedral angle between these rings is 83°, similar to that

* Lists of geometric details, structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43526 (40 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Erythrosine B atomic coordinates* (× 10⁴) *and equivalent isotropic thermal parameters* (× 10 Å²)

$$B_{eq} = \tfrac{4}{3}\sum_i\sum_j \beta_{ij}(\mathbf{a}_i\mathbf{a}_j).$$

	x	*y*	*z*	B_{eq}
I(1)	7142 (1)	1421 (1)	3263 (1)	28 (1)
I(3)	4614 (1)	2516 (1)	5678 (1)	33 (1)
I(7)	10585 (1)	−4002 (1)	7046 (1)	43 (1)
I(9)	9552 (1)	−1276 (1)	3794 (1)	29 (1)
C(1)	6859 (9)	1193 (9)	4450 (7)	41 (3)
C(2)	6155 (9)	1906 (8)	4666 (7)	39 (3)
C(3)	5825 (10)	1633 (9)	5441 (8)	44 (3)
C(4)	6346 (11)	817 (9)	5970 (7)	44 (4)
C(4*A*)	7150 (9)	173 (8)	5792 (6)	38 (3)
C(5)	7737 (9)	−625 (6)	6348 (7)	38 (3)
C(5*A*)	8472 (9)	−1266 (8)	6075 (7)	40 (3)
C(6)	9073 (10)	−2106 (9)	6590 (7)	43 (3)
C(7)	9761 (11)	−2705 (9)	6285 (8)	49 (4)
C(8)	9939 (10)	−2485 (8)	5494 (7)	42 (3)
C(9)	9302 (9)	−1650 (8)	4980 (7)	41 (3)
C(9*A*)	8638 (10)	−1069 (8)	5288 (7)	39 (3)
O(10)	8049 (7)	−259 (5)	4745 (5)	53 (2)
C(1*A*)	7374 (9)	374 (8)	4995 (7)	39 (3)
C(11)	7474 (9)	−910 (9)	7137 (7)	41 (3)
C(12)	7969 (11)	−434 (9)	7978 (8)	47 (4)
C(13)	7611 (11)	−709 (10)	8672 (8)	50 (4)
C(14)	6804 (14)	−1462 (11)	8546 (10)	63 (5)
C(15)	6306 (13)	−1955 (11)	7733 (9)	57 (5)
C(16)	6655 (13)	−1673 (11)	7048 (9)	60 (5)
C(17)	8883 (11)	341 (9)	8123 (9)	52 (4)
O(171)	9151 (10)	808 (9)	8913 (7)	87 (4)
O(172)	9348 (9)	534 (8)	7592 (6)	78 (4)
O(2)	5794 (9)	2719 (8)	4217 (7)	59 (3)
O(8)	10598 (8)	3021 (8)	5176 (6)	66 (3)
O(1*)	7499 (9)	4150 (8)	4152 (8)	84 (4)
C(2*)	7097 (17)	5089 (15)	3731 (20)	95 (10)
C(3*)	7829 (23)	5928 (24)	4267 (32)	154 (17)

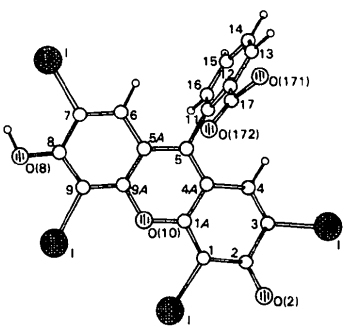

Fig. 1. Molecular conformation and numbering scheme for erythrosine B.

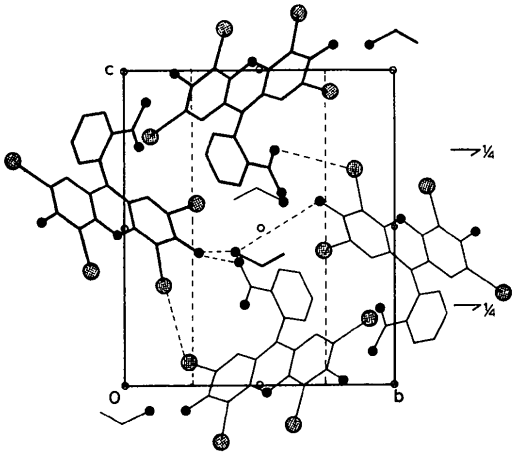

Fig. 2. Crystal packing of erythrosine B ethanolate projected along the *a* axis. The filled circles are oxygen and the stippled circles are iodine. The hydrogen bonding and short intermolecular I···I and I···O contacts are shown.

observed in the crystal structure of fluorescein perchlorate (Dubost, Leger, Colleter, Levillain & Fompeydie, 1981) and its lactoid form (Osborn & Rogers, 1975). The geometry of the xanthene ring system is consistent with a tautomer form in which the dye is a free acid with a keto oxygen at O(2) and a hydroxyl oxygen at O(8). The xanthene ring is folded 6° along the O(10)–C(5) bond and is more puckered than the perchlorate structure (2°). The carboxylic acid group is nearly coplanar (8°) with the benzene ring. This conformation is the same as that observed in the structure of fluorescein (Dubost *et al.*, 1981) and as found in the protein structure of the lactate dehydrogenase–erythrosine B binary complex (Wassarman & Lentz, 1971).

There are hydrogen bonds between O(8) of the dye and the hydroxyl oxygen of ethanol and between the carboxylic oxygen O(171) and O(172). As is frequently observed in thyroid hormone structures (Cody, 1980), there are short I···I [3·825 (1)] and I···O [3·196 (1) Å] van der Waals contacts in this structure (Fig. 2).

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References

CODY, V. (1980). *Endocrine Rev.* **1**, 140–162.

CODY, V. (1985). *Endocrine Res.* **11**, 211–224.

DETITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. A. (1975). *Acta Cryst.* A**31**, 472–479.

DUBOST, J. P., LEGER, J. M., COLLETER, J. C., LEVILLAIN, P. & FOMPEYDIE, D. (1981). *C. R. Acad. Sci. Paris Sér.* II, **292**, 965–968.

Enraf–Nonius (1979). *Structure Determination Package.* Enraf–Nonius, Delft.

FEKKES, D., HENNEMANN, G. & VISSER, T. J. (1982). *Biochem. J.* **201**, 673–676.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

LEVITAN, H. (1977). *Proc. Natl Acad. Sci. USA*, **74**, 2914–2918.

MOL, J. A., DOCTER, R., HENNEMANN, G. & VISSER, T. J. (1982). *Biochem. Biophys. Res. Commun.* **120**, 28–36.

OSBORN, R. S. & ROGERS, D. (1975). *Acta Cryst.* B**31**, 359–364.

RUIZ, M. & INGBAR, S. H. (1982). *Endocrinology*, **110**, 1613–1617.

SMITH, P. A., DOMBRO, K. & ZIDICHOUSKI, J. (1984). *J. Pharmacol. Exp. Ther.* **230**, 221–227.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination.* New York: Macmillan.

VOUGHT, R. L., BROWN, F. A. & WOLFF, J. (1972). *J. Clin. Endocrinol.* **34**, 747–752.

WASSARMAN, P. M. & LENTZ, P. J. JR. (1971). *J. Mol. Biol.* **60**, 509–522.

Acta Cryst. (1987). C**43**, 707–711

Structures of Two Inactive Nifedipine Analog Calcium Channel Antagonists: (I) $C_{17}H_{17}N_3O_4$ and (II) $C_{19}H_{20}N_2O_6$

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Abstract. (I): Ethyl 5-cyano-2,6-dimethyl-4-(2-nitrophenyl)-1,4-dihydropyridine-3-carboxylate, $C_{17}H_{17}N_3O_4$, $M_r = 327{\cdot}34$, monoclinic, $P2_1/c$, $a = 7{\cdot}983$ (2), $b = 15{\cdot}614$ (4), $c = 13{\cdot}405$ (4) Å, $\beta = 100{\cdot}54$ (3)°, $V = 1643$ (1) Å^3, $Z = 4$, $D_x = 1{\cdot}32$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71073$ Å, $\mu = 0{\cdot}90$ cm^{-1}, $F(000) = 688$, $T = 295$ K, $R = 0{\cdot}051$ for 2319 observed reflections. (II): Dimethyl 2,6-dimethyl-4-[*trans*-(2-nitrophenyl)-

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