plane previously defined of the atoms H(2) and H(9) being 1·230 (7) and 1·228 (8) Å respectively. On the other hand, the distances of the atoms H(9) and H(10) to this plane, 1·228 (8) and −1·212 (7) Å respectively, confirm the *trans* relationship between the C(9)—H(9) and C(10)—H(10) bonds. The C(2) phenyl group occupies an equatorial position as shown by the distance of C(17) to this least-squares plane of −0·194 (6) Å.

The N-atom geometry is tetrahedral rather than planar. The position of the N(1) phenyl plane is given by the torsion angle C(2)—N(1)—C(11)—

C(12) of −120·4 (6)°. The dihedral angle between the N(1) phenyl ring and the C(2) phenyl ring is 68 (1)°.

References

FRENZ, B. A. (1985). *Enraf–Nonius SDP Structure Determination Package*. Version 3.0. Enraf–Nonius, Delft, The Netherlands.
JOHNSON, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN*11/82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

Structure of the 4-Oxo-2-butenoic Acid Alkyl Ester Moiety. III. Structures of Diethyl N,N'-(Ethylenediamino)bis(4-oxo-2-butenoate) and Propyl 4-Oxo-4-ureido-2-butenoate
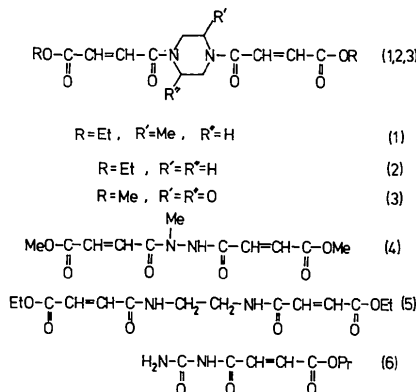
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Abstract. (5), $C_{14}H_{20}N_2O_6$, $M_r = 312·3$, monoclinic, $P2_1/c$, $a = 11·348$ (1), $b = 4·854$ (1), $c = 14·629$ (1) Å, $\beta = 99·87$ (1)°, $V = 793·9$ Å^3, $Z = 2$, $D_x = 1·306$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, Ni filter, $\mu = 0·83$ mm^{-1}, $F(000) = 332$, $T = 293$ K, $R = 0·047$ for 755 reflections. (6), $C_8H_{12}N_2O_4$, $M_r = 200·2$, orthorhombic, *Pccn*, $a = 39·365$ (2), $b = 10·147$ (1), $c = 9·937$ (1) Å, $V = 3968·9$ Å^3, $Z = 16$, $D_x = 1·340$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, Ni filter, $\mu = 0·93$ mm^{-1}, $F(000) = 1696$, $T = 293$ K, $R = 0·043$ for 2119 reflections. The conjugated 4-amino-4-oxo-2-butenoate fragments are approximately planar, with the ester group *anti* to the double bond. Amide type NH···O hydrogen bonds join molecules into chains in the first structure. Crystals of the urea derivative contain a complex hydrogen-bonding network which includes an intramolecular hydrogen bond.

Introduction. In our studies of alkyl 4-oxo-2-butenoate structures (Główka & Iwanicka, 1990; Główka, Iwanicka & Najman, 1991) we try to analyse conformation and to estimate the flexibility of the chain fragment with a view to attaining a better understanding of the potential cytostatic activity shown by similar compounds. The most pronounced inhibition of transplantable neoplasms L1210, P388 and Sa180 is shown by 4,4'-(2-methyl-1,4-piperazinediyl)bis(4-oxo-2-butenoic acid diethyl ester) (1) (Graczyk, Pakulska, Groszkowski &

Najman, 1980; Groszkowski & Najman, 1983) (see Scheme). As part of these studies we now describe the structures of the linear compounds (5) and (6).

Experimental. (5), (6). Data collection: CAD-4, $\omega/2\theta$ scan, $\theta_{max} = 75°$, three standards monitored every hour, absorption correction according to Walker & Stuart (1983), structure solution by direct methods, full-matrix least squares (non-H atoms anisotropic, H atoms isotropic), function minimized $\sum w(|F_o| - |F_c|)^2$; atomic scattering factors from analytical approximation in *SHELX*76; programs used: *SHELX*76 (Sheldrick, 1976), *SHELXS*86 (Sheldrick, 1986) and *ORTEP* (Johnson, 1976).

(5). Transparent, colourless prisms from aqueous ethyl acetate, crystal size $0.13 \times 0.08 \times 0.05$ mm; cell dimensions from 25 reflections in θ range 18–34°; data collection: h_{max}, k_{max}, $\pm l_{max}$ equal to 14, 6 and 18 respectively, 1923 reflections measured, 1625 unique ($R_{int} = 0.022$), only 755 observed with $I > 2.5\sigma(I)$, standards ($5\bar{1}3$, $40\bar{4}$ and $\bar{2}1\bar{5}$), less than 4% variation in intensity, max. and min. absorption corrections 1.49 and 0.67. Refinement: H atoms from difference Fourier synthesis, heavy-atom parameters (101 with scale and extinction) and H-atom parameters (42 with scale and extinction) were refined in separate blocks; $w^{-1} = \sigma^2(F_o) + 0.00006F_c^2$; refinement converged to a max. shift/e.s.d. $= 0.012$ for H atoms and 0.007 for non-H atoms, $R = 0.047$, $wR = 0.051$, $S = 2.16$. Max. and min. peaks in the final ΔF synthesis were 0.16 and -0.17 e Å^{-3}, isotropic extinction parameter $g = 0.006$ (Larson, 1967).

(6). Colourless prisms from acetone/ethanol, crystal size $0.24 \times 0.15 \times 0.07$ mm; cell dimensions from 25 reflections, θ range 21–28°; data collection: one octant, h_{max}, k_{max}, l_{max} equal to 49, 12 and 12 respectively, 4092 unique reflections measured, only 2119 observed with $I > 2\sigma(I)$, less than 5% variation in intensity, max. and min. absorption corrections 2.09 and 1.12. Refinement: H atoms from difference Fourier map (in the propyl groups some H atoms located geometrically), the two independent molecules refined alternately. Final cycles have 176 parameters for one molecule, refinement converged to a max. Δ/σ ratio of 0.002, $w^{-1} = 1.54/\sigma^2(F_o) + 0.00027F_o^2$, $R = 0.043$, $wR = 0.046$, $S = 1.50$, isotropic extinction parameter $g = 0.0008$ (Larson, 1967), max. and min. electron density difference peaks 0.18 e Å^{-3}, 0.91 Å from O(205) and -0.15 e Å^{-3}.

The molecular conformations and atomic (non-H atoms) labelling schemes are shown in Figs. 1 and 2. The final atomic coordinates for non-H atoms and equivalent isotropic temperature factors are given in Tables 1 and 2,* and selected bond distances and angles for these atoms are listed in Table 3.

Discussion. The *trans* configuration at the C(3)=C(4) double bond in (5) and (6) expected from the synthesis conditions is confirmed, as are the *syn* orientations of all neighbouring carbonyl groups in relation to the C(3)=C(4) double bond. The same geometry has been found to predominate in other structures containing the *trans* 4-amino-4-oxo-2-butenoate fragment. The only exception is structure (2) (see

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53836 (16 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Scheme) where the torsion angle C(3)=C(4)—C(5)= O(5) is -170.9 (5)°, cf. 1.1 (6) and -3.1 (6)° in (3), 3.3 (4) and 16.0 (4)° in (4), -21.6 (5)° in (5), and -0.2 (6) and 0.1 (5)° in (6) (Table 3).

The characteristic planarity of the conjugated 4-amino-4-oxo-2-butenoate chain is usually preserved, though significant deviations are sometimes visible, perhaps due to packing forces: e.g. the C(3)=C(4)—C(5)=O(5) torsion angle is 21.6° in (5). Corresponding bond lengths in 4-oxo-2-butenoate fragments do not differ by more than 0.02 Å, except for N(1)—C(2) which shows extreme values of 1.331 (2) Å in the hydrazine derivative (4) (Główka, Iwanicka & Najman, 1991) and 1.403 (4) Å in the 2,5-dioxo-1,4-piperazine derivative (3) (Główka & Iwanicka, 1990). The difference (0.07 Å) is due to extended conjugation involving the amide group in the latter structure. Differentiation of bond angles reaches 6.0° and it is connected with packing forces and the different surroundings of the N(1) atom.

The hydrogen-bond networks are formed mainly by the flat amide groups and do not obstruct the planarity of the molecule. In (5) there is only one H atom capable of forming a strong hydrogen bond: the N(1)—H···O(2) contact involves N···O, H···O distances and an N—H···O angle of 2.983 (4), 2.21 (3) Å and 168 (3)°, respectively. The hydrogen bonds join molecules into infinite chains running in the [100] direction.

In (6), the situation is more complex due to the presence both of three H atoms attached to donor amino groups and of three carbonyl groups which are possible acceptors. Though the geometry and
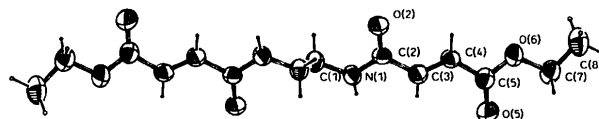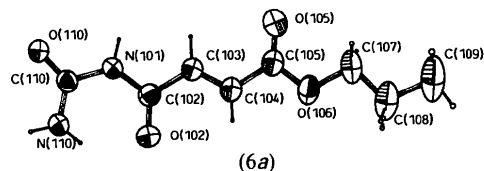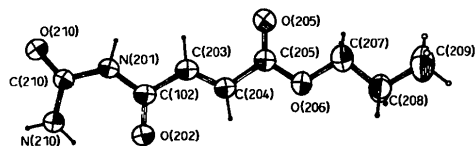

Fig. 1. A view of molecule (5) with labelling system used.

(6a)

(6b)

Fig. 2. A view of molecules (6a) and (6b) with labelling system used.

Table 1. *Final atomic coordinates and equivalent isotropic thermal parameters for compound* (5)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{eq}(\text{Å}^2)$
N(1)	0.0425 (3)	0.1488 (6)	0.1184 (2)	4.00 (8)
C(1)	−0.0341 (3)	0.0427 (8)	0.0372 (2)	4.00 (10)
C(2)	0.1009 (3)	−0.0184 (7)	0.1844 (2)	3.58 (8)
O(2)	0.0935 (2)	−0.2699 (5)	0.1786 (2)	4.73 (8)
C(3)	0.1751 (3)	0.1276 (7)	0.2629 (2)	4.07 (10)
C(4)	0.2343 (3)	0.0020 (7)	0.3365 (2)	3.89 (10)
C(5)	0.3021 (3)	0.1658 (8)	0.4128 (2)	4.11 (10)
O(5)	0.3365 (3)	0.3962 (5)	0.4056 (2)	6.11 (9)
O(6)	0.3209 (2)	0.0242 (6)	0.4919 (2)	5.16 (8)
C(7)	0.3838 (4)	0.1712 (9)	0.5736 (3)	5.57 (13)
C(8)	0.4013 (4)	−0.0277 (11)	0.6523 (3)	6.54 (14)

Table 2. *Final positional and equivalent isotropic thermal parameters for compound* (6)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{eq}(\text{Å}^2)$
(6a)				
N(101)	0.4184 (1)	0.7245 (2)	0.1432 (2)	3.48 (6)
C(102)	0.4029 (1)	0.6304 (2)	0.2193 (3)	3.57 (8)
O(102)	0.4080 (1)	0.5122 (2)	0.2062 (2)	4.94 (6)
C(103)	0.3786 (1)	0.6828 (3)	0.3199 (3)	3.83 (8)
C(104)	0.3599 (1)	0.6058 (3)	0.3953 (3)	4.19 (8)
C(105)	0.3353 (1)	0.6624 (3)	0.4921 (3)	4.65 (9)
O(105)	0.3305 (1)	0.7770 (2)	0.5100 (3)	7.71 (10)
O(106)	0.3188 (1)	0.5681 (2)	0.5589 (2)	5.35 (6)
C(107)	0.2949 (1)	0.6142 (5)	0.6601 (5)	6.25 (13)
C(108)	0.2765 (1)	0.4988 (5)	0.7137 (4)	7.01 (15)
C(109)	0.2513 (2)	0.5402 (9)	0.8235 (6)	9.74 (21)
C(110)	0.4406 (1)	0.7081 (2)	0.0324 (3)	3.32 (6)
O(110)	0.4507 (1)	0.8082 (2)	−0.0264 (2)	3.98 (5)
N(110)	0.4487 (1)	0.5867 (2)	−0.0005 (3)	4.22 (7)
(6b)				
N(201)	0.5279 (1)	0.6021 (2)	−0.3900 (2)	3.61 (6)
C(202)	0.5481 (1)	0.6855 (2)	−0.4624 (3)	3.52 (7)
O(202)	0.5478 (1)	0.8056 (2)	−0.4493 (2)	4.84 (6)
C(203)	0.5703 (1)	0.6167 (3)	−0.5597 (3)	3.83 (8)
C(204)	0.5883 (1)	0.6770 (3)	−0.6506 (3)	3.73 (7)
C(205)	0.6088 (1)	0.5992 (3)	−0.7459 (3)	3.74 (7)
O(205)	0.6101 (1)	0.4799 (2)	−0.7459 (2)	5.50 (7)
O(206)	0.6260 (1)	0.6739 (2)	−0.8321 (2)	4.49 (5)
C(207)	0.6444 (1)	0.6049 (4)	−0.9369 (4)	4.98 (10)
C(208)	0.6687 (1)	0.6984 (4)	−1.0007 (4)	5.49 (10)
C(209)	0.6863 (2)	0.6318 (6)	−1.1182 (6)	8.50 (18)
C(210)	0.5043 (1)	0.6307 (2)	−0.2888 (3)	3.37 (7)
O(210)	0.4885 (1)	0.5385 (2)	−0.2400 (2)	4.94 (6)
N(210)	0.5007 (1)	0.7750 (2)	−0.2529 (3)	3.79 (6)

conformation of (6*a*) and (6*b*), the two independent molecules of (6), are very similar, their environments are not: (6*a*) acts as an acceptor in three hydrogen bonds and (6*b*) participates in five such bonds. The planarity of the molecules harmonizes with intramolecular N(10)—H···O(2) hydrogen bonds. N···O distances are 2·712 (4) and 2·740 (5) Å, H···O distances 2·06 (3) and 2·12 (3) Å, and N—H···O angles 135 (3) and 128 (3)°, respectively for (6*a*) and (6*b*). The same H atoms participate in intermolecular hydrogen bonds: N(110)—H···O(202) [1 − x, y − ½, −z − ½; N···O and O···H 2·899 (3) and 2·46 (3) Å, ∠N—H···O 113 (3)°] and N(210)—H···O(210) [1 − x,

Table 3. *Selected bond lengths* (Å) *and angles* (°) *in 'linear' alkyl esters of 4-amino-4-oxo-2-butenoates*

	(5)	(6a)	(6b)	(4a)*	(4b)*
N(1)—C(2)	1·346 (4)	1·362 (4)	1·366 (4)	1·361 (3)	1·331 (2)
C(2)—O(2)	1·226 (4)	1·223 (3)	1·226 (3)	1·212 (3)	1·220 (3)
C(2)—C(3)	1·483 (4)	1·482 (5)	1·478 (5)	1·492 (3)	1·483 (3)
C(3)—C(4)	1·317 (4)	1·309 (5)	1·301 (5)	1·307 (3)	1·313 (4)
C(4)—C(5)	1·475 (4)	1·481 (5)	1·474 (5)	1·491 (4)	1·473 (4)
C(5)—O(5)	1·195 (5)	1·191 (4)	1·212 (4)	1·193 (3)	1·203 (3)
C(5)—O(6)	1·331 (4)	1·333 (4)	1·329 (4)	1·314 (3)	1·320 (3)
O(6)—C(7)	1·468 (5)	1·454 (5)	1·449 (5)	1·453 (3)	1·438 (4)
N(1)—C(2)—C(3)	114·3 (3)	114·3 (2)	113·3 (2)	117·4 (2)	115·3 (2)
N(1)—C(2)—O(2)	122·1 (3)	123·7 (3)	123·7 (3)	120·1 (2)	121·9 (2)
O(2)—C(2)—C(3)	123·6 (3)	122·0 (2)	123·0 (2)	122·5 (2)	122·8 (2)
C(2)—C(3)—C(4)	123·7 (3)	122·3 (3)	123·6 (3)	120·7 (2)	122·1 (2)
C(3)—C(4)—C(5)	119·7 (3)	120·5 (3)	119·5 (3)	121·1 (2)	121·4 (2)
C(4)—C(5)—O(5)	125·0 (3)	125·4 (3)	123·9 (3)	124·3 (2)	124·9 (2)
C(4)—C(5)—O(6)	111·4 (3)	111·3 (3)	112·8 (3)	111·6 (2)	111·8 (2)
O(5)—C(5)—O(6)	123·6 (3)	123·3 (3)	123·2 (3)	124·1 (2)	123·3 (2)
C(5)—O(6)—C(7)	116·1 (3)	115·4 (3)	116·3 (3)	116·1 (2)	116·7 (2)
C—N(1)—C(2)—C(3)	−179·8 (3)	−174·5 (3)	179·0 (3)		
C—N(1)—C(2)—O(2)	1·0 (5)	4·8 (5)	−1·5 (5)		
N(1)—C(2)—C(3)—C(4)	176·5 (3)	175·5 (3)	170·9 (3)	174·0 (2)	−160·1 (2)
O(2)—C(2)—C(3)—C(4)	−4·3 (5)	−3·8 (5)	−8·6 (5)	−9·1 (4)	17·1 (3)
C(2)—C(3)—C(4)—C(5)	−177·7 (3)	−178·4 (3)	−178·0 (3)	176·4 (2)	178·1 (2)
C(3)—C(4)—C(5)—O(5)	−21·6 (5)	−0·2 (6)	0·1 (5)	3·3 (4)	16·0 (4)
C(3)—C(4)—C(5)—O(6)	158·5 (3)	180·0 (3)	−179·5 (3)	−175·2 (2)	−161·4 (2)
C(4)—C(5)—O(6)—C(7)	−177·8 (3)	177·9 (3)	−174·6 (3)	180·0 (2)	179·6 (2)
O(5)—C(5)—O(6)—C(7)	2·3 (5)	−2·0 (5)	5·7 (5)	1·6 (4)	2·2 (4)

* Głowka, Iwanicka & Najman (1991).

$y + \frac{1}{2}$, $-z - \frac{1}{2}$; N···O and O···H 2·908 (3) and 2·25 (3) Å, ∠N—H···O 132 (3)°]. The other H atom of the terminal amide groups forms hydrogen bonds N(110)—H′···O(210) and N(210)—H′···O(110) with distances of 2·891 (4) and 3·038 (4) Å for N···O, 2·01 (4) and 2·22 (4) Å for H···O, and N—H···O angles of 172 (3) and 172 (3)°. Two other intermolecular hydrogen bonds are formed by N(1)—H groups: N(101)—H···O(205) (1 − x, y + ½, −z − ½) and N(201)—H···O(110) (1 − x, y + ½, −z − ½), characterized by the N···O, H···O, N—H···O values of 3·002 (3), 2·14 (3) Å and 166 (3)° for the (6*a*) and 3·208 (3), 2·35 (3) Å and 172 (3)°, respectively, for (6*b*).

References

Głowka, M. L. & Iwanicka, I. (1990). *Acta Cryst.* C46, 1262–1264.

Głowka, M. L., Iwanicka, I. & Najman, L. (1991). *Acta Cryst.* C47, 618–620.

Graczyk, J., Pakulska, W., Groszkowski, S. & Najman, L. (1980). *Acta Polon. Pharm.* 37, 249–254.

Groszkowski, S. & Najman, L. (1983). *Pol. J. Pharmacol. Pharm.* 35, 517–521.

Johnson, C. K. (1976). *ORTEPII.* Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

LARSON, A. C. (1967). *Acta Cryst.* **23**, 664–665.
SHELDRICK, G. M. (1976). *SHELX76.* Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1986). *SHELXS86.* Program for the solution of crystal structures. Univ. of Göttingen, Germany.
WALKER, N. & STUART, D. (1983). *Acta Cryst.* A**39**, 158–166.

Structure of a Psoralen Derivative of a Monosubstituted 18-Crown-6 Ether

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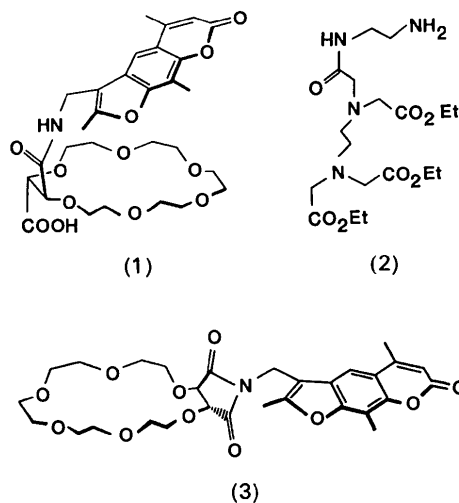**Abstract.** N-[(2,5,9-Trimethyl-7-oxo-7H-furo[3,2-g]-[1]benzopyran-3-yl)methyl]-1,4,7,10,13,16-hexaoxa-cyclooctadecane-2,3-dicarboximide, $C_{29}H_{35}NO_{11}$, M_r = 573·60, monoclinic, $P2_1$, a = 18·877 (9), b = 6·888 (6), c = 24·488 (10) Å, β = 119·90 (4)°, V = 2760·2 Å^3, Z = 4, D_x = 1·380 Mg m^{-3}, λ(Cu $K\bar{\alpha}$) = 1·54178 Å, μ = 0·85 mm^{-1}, $F(000)$ = 1216, T = 170 K, R = 0·065, wR = 0·057 for 3720 observed reflections. There are two molecules (I and II) in the asymmetric unit and the 18-crown-6 part of molecule II is disordered. The psoralen moieties of the two molecules are nearly centrosymmetrically related.

Introduction. The utilization of psoralens in medicine started more than 3000 years ago for the treatment of vitiligo and psoriasis, two skin deseases, and has been practised ever since (Parrish, Fitzpatrick, Tanenbaum & Pathak, 1974; Scott, Pathak & Mohn, 1976). In recent years, psoralen derivatives have been applied to the treatment of certain forms of skin cancer (Edelson, 1986, 1987). The successful use of psoralens in medicine has been linked to their ability to cross-link adjacent pyrimidine bases on two strands of the DNA double helix upon irradiation (Scott *et al.*, 1976; Haran & Crothers, 1978). In this context, psoralen molecules and derivatives have been used for a number of years as aromatic intercalants to probe nucleic acid structure, damage and repair, and more importantly, recombination through their involvement in photocross-linking to DNA upon irradiation by ultraviolet light (Saffran, Goldenberg & Cantor, 1982; Goldenberg, Welsh, Haas, Rideout & Cantor, 1988).

Owing to the growing interest in the design of photochemical DNA cleaving molecules we have developed the synthesis of a series of mono- and

bis-intercalant crown ethers having either a methidium or a psoralen function covalently attached to the macrocyclic ring with well defined stereochemistry (Basak & Dugas, 1986). More recently, an iron complex substituted psoralen has been prepared by Nakamura as a new photochemical DNA cleaver (Nakamura, 1989). It behaves as a model for bleomycin, one of the most potent antitumor antibiotic agents known.

In our own effort to develop a bleomycin model based on our psoralen–18-crown-6 monoacid (1), we coupled this chiral crown ether (Basak & Dugas, 1986) to the EDTA derivative (2) (Taylor, Schultz & Dervan, 1984); the EDTA side chains of this adduct will serve to bind iron and oxygen (Nakamura, 1989). However, during this synthesis a side reaction always took place between the acid and the amide function of psoralen–18-crown-6 monoacid (1) resulting in the corresponding cyclic imide (3). In the present paper we present the crystal structure determination of this novel psoralen–imido-18-crown-6 molecule.

(1)   (2)

(3)

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