Tetrahedron Vol 33, pp 2693 to 2697 Pergamon Press 1977 Printed in Great Britain

THE MOLECULAR STRUCTURE OF 3^a-METHOXY-9^a-METHOXYCARBONYL-1,3,4-TRIMETHYL-2-OXO-2,3,3^a,4,9,9^a-HEXAHYDRO-1H-IMIDAZO[4,5-B]QUINOXALINE AND OF 4^a,10^a-ETHYLENEDIOXY-1,3,10-TRIMETHYL-4^a,5,10,10^a-TETRAHYDROALLOXAZINE

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(*Received in UK* 17 *January* 1977; *accepted for publication* 18 *April* 1977)

Abstract—The molecular structure of two adducts derived from 1,3,10-trimethyl-alloxazinium cation with methanol and glycol respectively has been determined by X-ray analysis. The first compound was identified as a 1H-imidazo[4,5-b]-quinoxaline ring system indicating a transformation of the original alloxazine ring system and reactivity at the C4 site in the 1,3,10-trimethylalloxazinium cation on formation of the intermediate dimethoxy adduct. The final R-index is 5.3% using 2658 non-zero reflexions.

The structure of the second compound implies that the original alloxazine framework is retained and that only one ethylenedioxy-ion is involved in the reaction. The final R-index is 4.8% using 1406 non-zero reflexions.

In course of an investigation on activation and transfer of oxygen the structures and rearrangements of adducts derived from 1,3,10-trimethylalloxazinium cation and mono- and di-hydric alcohols were studied.[1]

During this study the question arose whether monohydric alcohol adduct formation of **1** (Scheme 1; R = Me) would finally lead to structure **2b** or **3** (**5a** or **5c** in Mager's paper).

From spectroscopic measurements it was impossible to determine the correct frame work conclusively. X-ray analysis of the reaction product (hereafter called: MONO) revealed the correct structural formula **2b**.

In continuation it was questioned whether the same type of ringcontraction takes place in adducts of **1** and dihydric alcohols.

This rearrangement of the alloxazine frame work during the reaction with glycol might proceed via **2a**→**2b**→**2d**, or after the attack of a second hydroxyethyleneoxide ion in **2a** at C4 (Scheme 2). The last pathway was rejected on basis of elemental analysis.

From spectroscopic measurements it was impossible to decide whether product **2c** or **2d** (**6c** or **6d** in Mager's paper) was formed. Therefore this X-ray analysis of the reaction product (hereafter called: Di) was started.

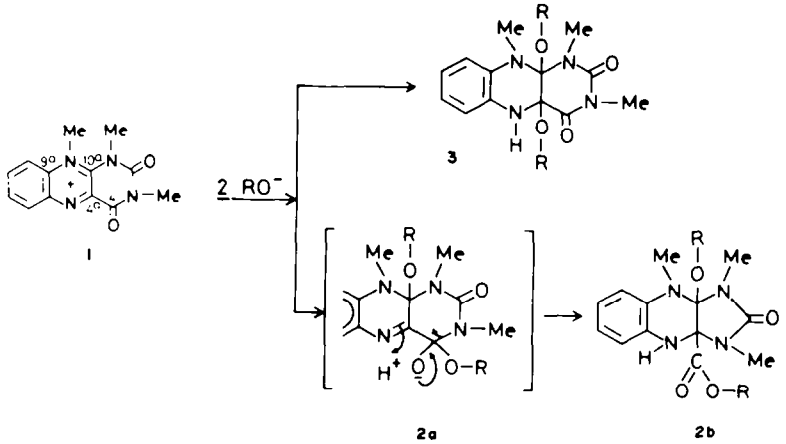
EXPERIMENTAL

Samples of the compounds, $C_{15}H_{20}N_4O_4$ (MONO) and $C_{15}H_{18}N_4O_4$ (Di), were kindly provided by H. I. X. Mager from the Biochemical and Biophysical Laboratory of the Delft University of Technology.

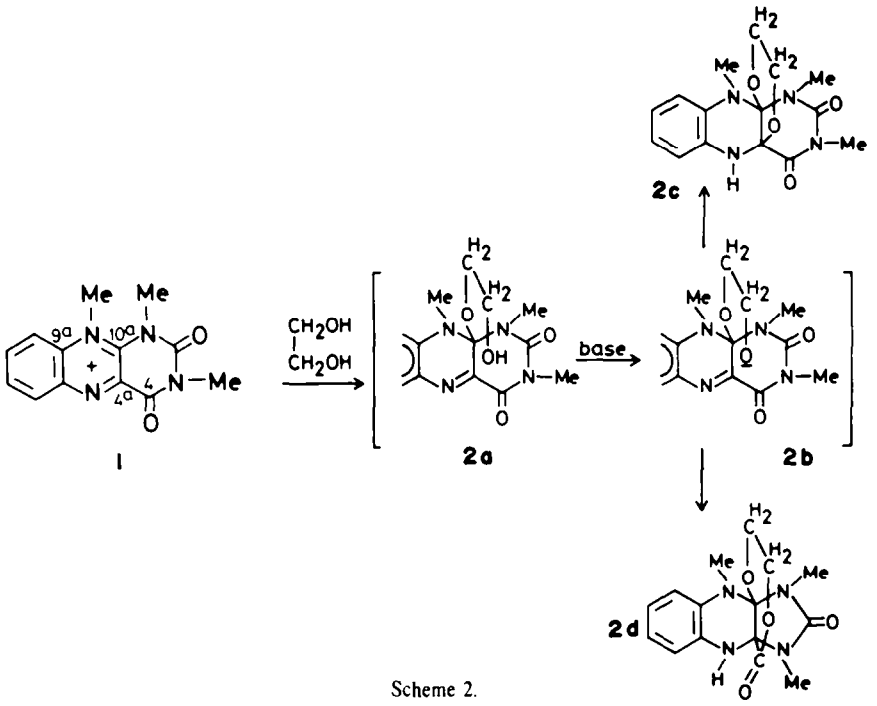
Crystals of MONO were grown from methanol solution at room temp. The crystals are monoclinic, space group $P2_1/c$ with a = 7.908 (2), b = 11.940 (4), c = 17.490 (6), β = 105.27 (3) and Z = 4. Three dimensional intensity data were collected with the CAD3-Nonius diffractometer using CuK_α radiation and the $\theta/2\theta$-scan mode with a maximum θ-value of 68.10°.

Rhombic crystals of Di, space group Pbca with a = 24 174 (9), b = 7.189 (3), c = 16.837 (5) Å and Z = 8, were obtained by recrystallization from methanol at 5°C. Intensities were collected up to θ = 26.00° with the CAD3-Nonius diffractometer using MoK_α radiation. In reduction of the intensities to F and E values no absorption correction was made.

Structure determination. The structures were solved using direct methods. The E-maps did reveal all heavy atoms. After blocked full-matrix refinement the positions of the hydrogen atoms were obtained from difference synthesis. The last cycle of blocked full-matrix anisotropic least-squares refinement, with fixed isotropic thermal parameters for the H atoms, converged to the conventional R = 5.3% using 2658 observed (non-zero) reflexions (MONO) and to R = 4.8% using 1406 non-zero reflexions (Di) with omission of 4 very strong low-order reflexions. The



Scheme 1.



Scheme 2.

Table 1. Final parameters in MONO with e.s.d.'s in parentheses. The fractional atomic coordinates are multiplied by 10^4 for the non-hydrogen atoms and by 10^3 for the hydrogen atoms. The expression for the anisotropic thermal parameters ($Å^2 \times 10^3$) is:

$$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + a^*b^*khU_{12} + b^*c^*klU_{23} + c^*a^*lhU_{31})]$$

The isotropic factors (U) are in $Å^2 \times 10^3$.

Atom	x/a	y/b	z/c	U_{11}/U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C1	6586(3)	3600(2)	1789(2)	30(1)	30(1)	39(1)	1(1)	4(1)	-4(1)
C2	6079(4)	3935(2)	1004(2)	48(2)	44(2)	40(2)	-2(1)	2(1)	0(1)
C3	4934(5)	3275(3)	442(2)	60(2)	71(2)	39(2)	-6(2)	-3(2)	-8(2)
C4	4342(5)	2283(3)	667(2)	55(2)	66(2)	54(2)	-17(2)	-2(2)	-24(2)
C5	4856(4)	1940(2)	1453(2)	44(2)	41(2)	63(2)	-14(1)	11(2)	-13(2)
C6	5975(3)	2593(2)	2028(2)	27(1)	31(1)	45(1)	3(1)	7(1)	-5(1)
C7	5757(4)	1273(3)	3081(2)	43(2)	44(2)	75(2)	-12(1)	19(2)	11(2)
C8	7947(3)	2773(2)	3388(2)	32(1)	27(1)	41(1)	4(1)	8(1)	2(1)
C9	8871(3)	3658(2)	2982(1)	27(1)	27(1)	34(1)	2(1)	3(1)	0(1)
C10	10565(4)	2054(2)	3234(2)	36(1)	32(1)	49(2)	3(1)	6(1)	-6(1)
C11	11366(4)	3429(3)	2342(2)	44(2)	65(2)	63(2)	-6(2)	23(2)	2(2)
C12	9601(5)	1202(3)	4327(2)	64(2)	47(2)	56(2)	12(2)	8(2)	21(2)
C13	5975(5)	3805(3)	3973(2)	66(2)	56(2)	73(2)	25(2)	35(2)	8(2)
C14	9953(4)	4406(2)	3629(2)	38(1)	34(1)	36(1)	-2(1)	3(1)	3(1)
C15	10253(5)	6281(3)	4157(2)	90(3)	44(2)	57(2)	-5(2)	-12(2)	-19(2)
N1	7655(3)	4259(2)	2384(1)	35(1)	24(1)	38(1)	-4(1)	-1(1)	3(1)
N2	6411(3)	2328(2)	2831(1)	35(1)	31(1)	48(1)	-7(1)	3(1)	3(1)
N3	10118(3)	2342(2)	2726(1)	30(1)	35(1)	41(1)	2(1)	10(1)	9(1)
N4	9348(3)	1946(2)	3649(1)	36(1)	31(1)	53(1)	12(1)	12(1)	13(1)
O1	11841(3)	1440(2)	3302(1)	43(1)	45(1)	75(1)	19(1)	13(1)	-5(1)
O2	7560(3)	3154(2)	4084(1)	44(1)	44(1)	41(1)	9(1)	15(1)	1(1)
O3	11301(3)	4197(2)	4081(1)	51(1)	56(1)	61(1)	9(1)	-2(1)	-9(1)
O4	9237(3)	5469(2)	3536(1)	60(1)	32(1)	46(1)	4(1)	-9(1)	-12(1)
H1	799(3)	486(2)	223(1)	31					
H21	662(4)	467(2)	87(2)	44					
H31	481(4)	306(2)	-11(2)	57					
H41	358(4)	134(2)	27(2)	57					
H51	445(4)	132(2)	162(2)	48					
H71	457(4)	125(2)	288(2)	55					
H72	591(4)	126(2)	373(2)	55					
H73	633(4)	56(2)	284(2)	55					
H111	1076(4)	374(2)	190(2)	59					
H112	1208(4)	401(2)	287(2)	59					
H113	1214(4)	281(2)	217(2)	59					
H121	886(4)	148(2)	471(2)	58					
H122	1026(4)	175(2)	463(2)	58					
H123	900(4)	45(2)	416(2)	58					
H131	491(4)	330(3)	392(2)	64					
H132	585(4)	432(3)	350(2)	64					
H133	614(4)	429(3)	449(2)	64					
H151	1033(4)	603(3)	456(2)	64					
H152	955(4)	667(3)	404(2)	64					
H153	1141(4)	643(3)	401(2)	64					

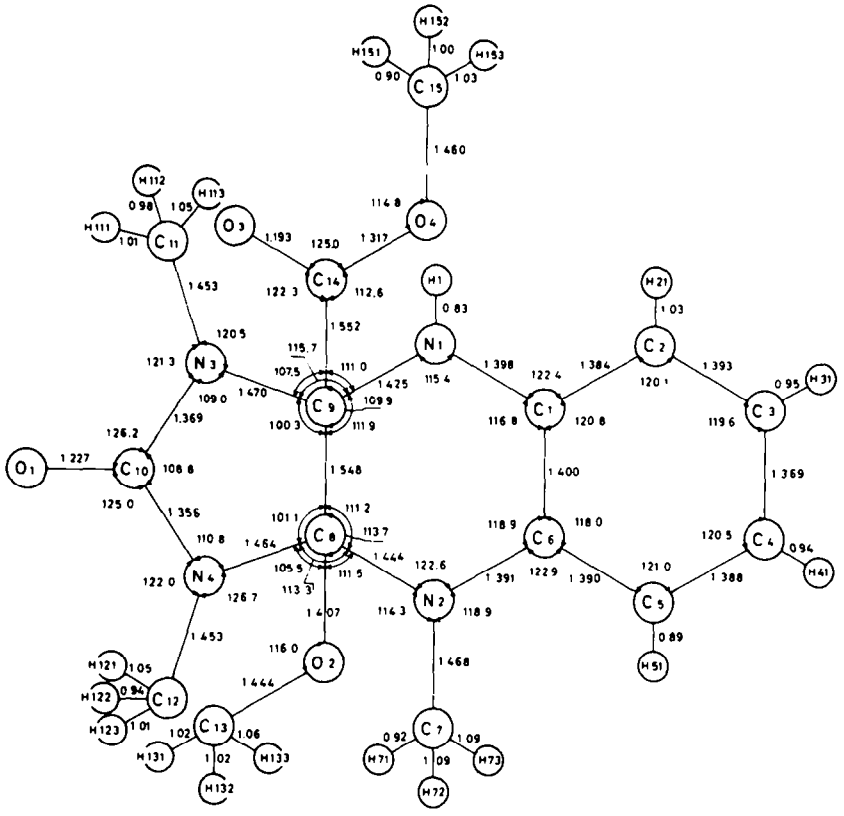


Fig. 1. Bond lengths (Å) and bond angles (°) in MONO. The estimated standard deviations (e.s.d.'s) are 0.004 Å for distances between non-hydrogen atoms and 0.03 Å for distances to hydrogen atoms. The e.s.d.'s of the angles given are around 0.2°.

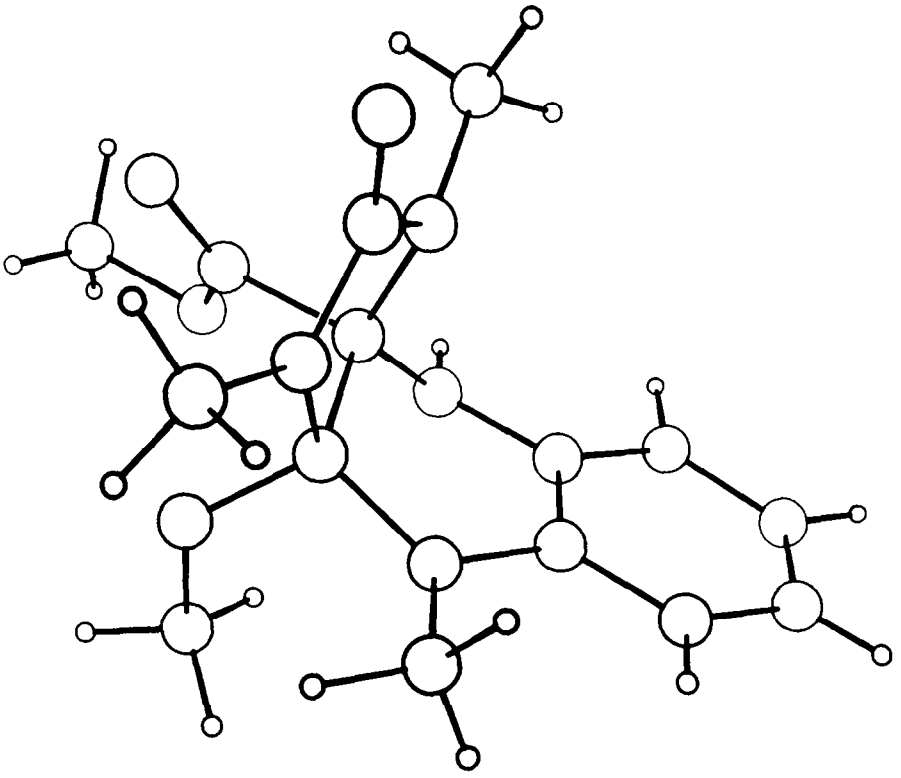


Fig. 2. ORTEP drawing of the molecule MONO.

Table 2. Final parameters in Di with e.s.d.'s in parentheses. The fractional atomic coordinates are multiplied by 10^4 for the non-hydrogen atoms and by 10^3 for the hydrogen atoms. The expression for the anisotropic thermal parameters ($Å^2 \times 10^3$) is:

$$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + a^*b^*khU_{12} + b^*c^*klU_{23} + c^*a^*lhU_{31}]$$

The isotropic factors (U) are in $Å^2 \times 10^3$.

Atom	x/a	y/b	z/c	U_{11}/U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C1	1130(2)	3719(6)	4659(2)	27(2)	38(2)	34(2)	3(2)	-1(2)	2(2)
C2	900(2)	4314(7)	5371(3)	38(2)	57(3)	45(3)	5(2)	11(2)	-3(3)
C3	1176(2)	5558(8)	5855(3)	56(3)	64(3)	45(3)	12(3)	6(2)	-22(3)
C4	1689(2)	6186(7)	5651(3)	59(3)	43(3)	56(3)	2(3)	-6(3)	-16(3)
C5	1930(2)	5630(6)	4944(3)	43(2)	33(2)	39(2)	-3(2)	-5(2)	0(2)
C6	1647(2)	4397(6)	4447(2)	30(2)	35(2)	28(2)	-1(2)	-3(2)	3(2)
C7	1048(1)	2230(5)	3357(2)	23(2)	32(2)	36(2)	-3(2)	-3(2)	3(2)
C8	1683(1)	2292(6)	3314(2)	21(2)	36(2)	31(2)	-1(2)	-3(2)	0(2)
C9	1080(2)	-1090(7)	3367(4)	42(3)	34(3)	75(4)	-5(2)	-2(3)	5(3)
C10	1694(2)	-1023(7)	3284(4)	43(3)	37(3)	79(4)	10(2)	2(3)	12(3)
C11	1889(2)	2469(6)	2461(2)	30(2)	31(2)	37(2)	-7(2)	1(2)	-6(2)
C12	1041(2)	4184(6)	2143(3)	36(2)	44(3)	45(3)	4(2)	-4(2)	8(2)
C13	1793(2)	3899(8)	1163(3)	52(3)	52(3)	35(3)	-12(3)	6(2)	-1(2)
C14	261(2)	4358(8)	3032(4)	30(2)	56(3)	68(4)	7(2)	1(2)	6(3)
C15	350(2)	1566(8)	4443(3)	36(3)	66(4)	53(3)	-20(3)	15(2)	0(3)
N1	875(1)	2399(5)	4172(2)	27(2)	44(2)	35(2)	-12(2)	6(1)	-1(2)
N2	1879(1)	3872(5)	3724(2)	28(2)	54(2)	38(2)	-17(2)	5(1)	-4(2)
N3	1561(1)	3445(5)	1950(2)	39(2)	34(2)	30(2)	-1(2)	2(2)	4(2)
N4	828(1)	3724(5)	2863(2)	25(2)	36(2)	41(2)	4(2)	-3(2)	5(2)
O1	1902(1)	642(4)	3663(2)	28(1)	44(2)	52(2)	1(1)	-6(1)	17(2)
O2	847(1)	573(4)	3016(2)	28(1)	35(2)	48(2)	-8(1)	-4(1)	-2(1)
O3	803(1)	5190(5)	1679(2)	62(2)	73(2)	65(2)	18(2)	-3(2)	30(2)
O4	2340(1)	1877(4)	2269(2)	33(2)	53(2)	47(2)	3(1)	9(1)	-6(2)
H2	218(2)	422(6)	363(2)	36					
H21	55(2)	385(6)	553(2)	43					
H31	104(2)	594(6)	637(3)	52					
H41	187(2)	701(6)	597(3)	52					
H51	232(2)	609(5)	476(2)	39					
H91	98(2)	-114(6)	392(3)	51					
H92	92(2)	-214(6)	306(2)	51					
H101	180(2)	-110(6)	268(3)	52					
H102	185(2)	-202(6)	357(3)	52					
H131	191(2)	267(6)	92(2)	46					
H132	214(2)	459(6)	123(2)	46					
H133	148(2)	440(6)	79(2)	46					
H141	0(2)	335(6)	307(3)	51					
H142	16(2)	524(6)	262(3)	51					
H143	25(2)	498(6)	359(3)	51					
H151	20(2)	78(6)	401(3)	55					
H152	6(2)	255(7)	457(2)	55					
H153	40(2)	87(6)	494(3)	55					

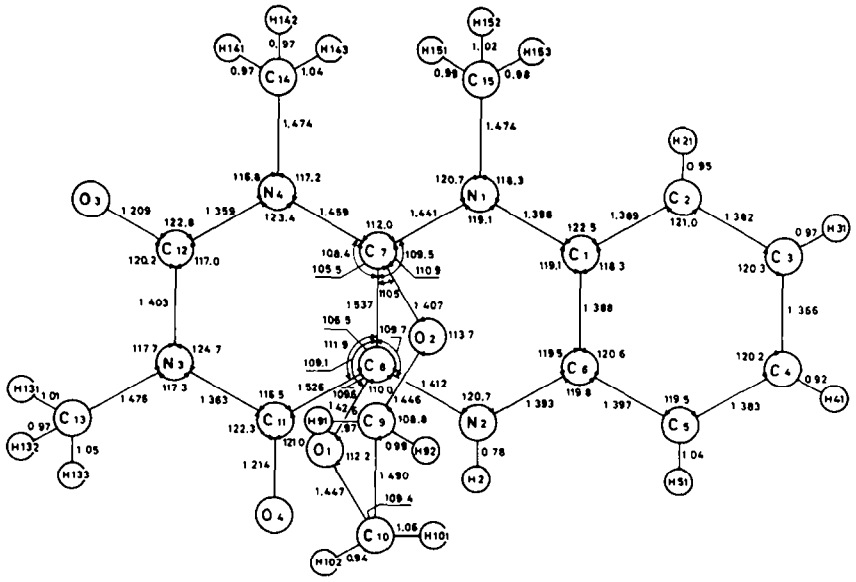


Fig. 3. Bond lengths (Å) and bond angles (°) in Di. The estimated standard deviations (e.s.d.'s) are 0.005 Å for distances between non-hydrogen atoms and 0.004 Å for distances to hydrogen atoms. The e.s.d.'s of the angles given are around 0.3°.

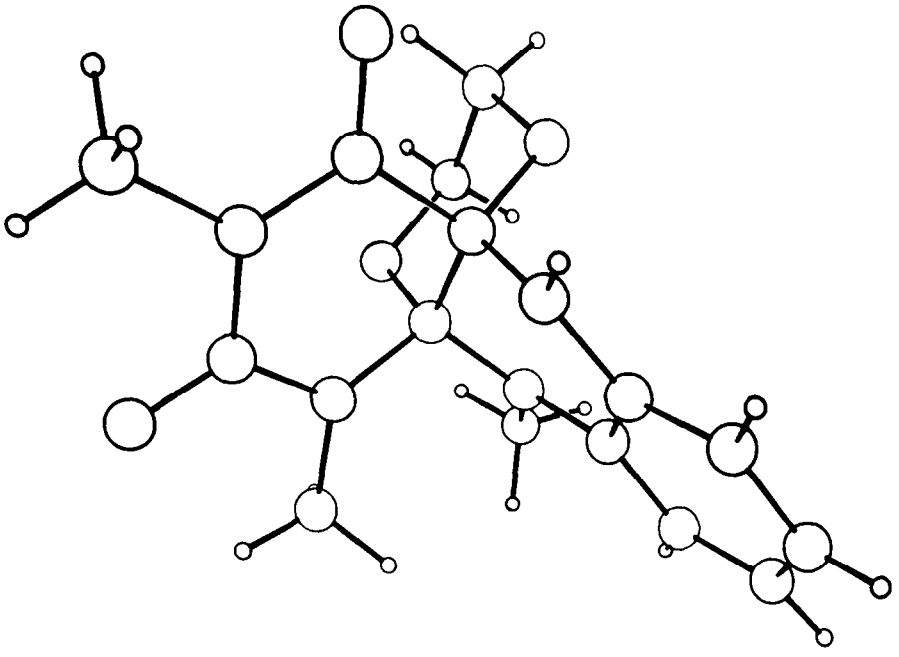


Fig. 4. ORTEP drawing of the molecule Di.

final difference maps did not show any special feature. The final atomic coordinates, the temperature factors and their standard deviations (e.s.d.'s) as calculated from the refinement are given in Tables 1 and 2. A list of F_0 and final F_c values is available from the laboratory.

All calculations were done using the "X-ray-system".[2]

RESULTS

Figure 1 shows the bond distances and bond angles in MONO. For the sake of clarity the bond angles involving H atoms are not included. An impression of the molecule is given in Fig. 2.

The X-ray analysis clearly indicates the transformation of the original alloxazine ring system into a fused imidazoquinoxaline ring system. The substituents on the bridge-C atoms are a OMe- and a methoxycarbonyl group respectively. Therefore, the reaction product investigated has the structural formula **2b** (R = Me). It is likely that the dimethoxy adduct **2a** is rearranged as indicated in Scheme 1 implying reactivity at the C4-site in **1**.

Figure 3 shows the bond distances and bond angles in Di. For the sake of clarity bond angles involving H atoms are not included.

An impression of the molecule is given in Fig. 4. The X-ray analysis shows that the original alloxazine ring system is not changed suggesting no reactivity at the C4 site in **1**. Only one molecule glycol is involved in the reaction; the bridge-C atoms $C4^a$ and $C10^a$, together with the ethylenedioxy moiety, form a chairlike 6-membered ring. The reaction product investigated has the structural formula 2^c.

REFERENCES

[1]H. I. X. Mager, *Tetrahedron* 33, 981 (1977).

[2]The X-ray System, Technical Report, 192 of the Comp. Sci. Center, University of Maryland, June (1972).