Hydrolysis Products of Flavins (Isoalloxazines)

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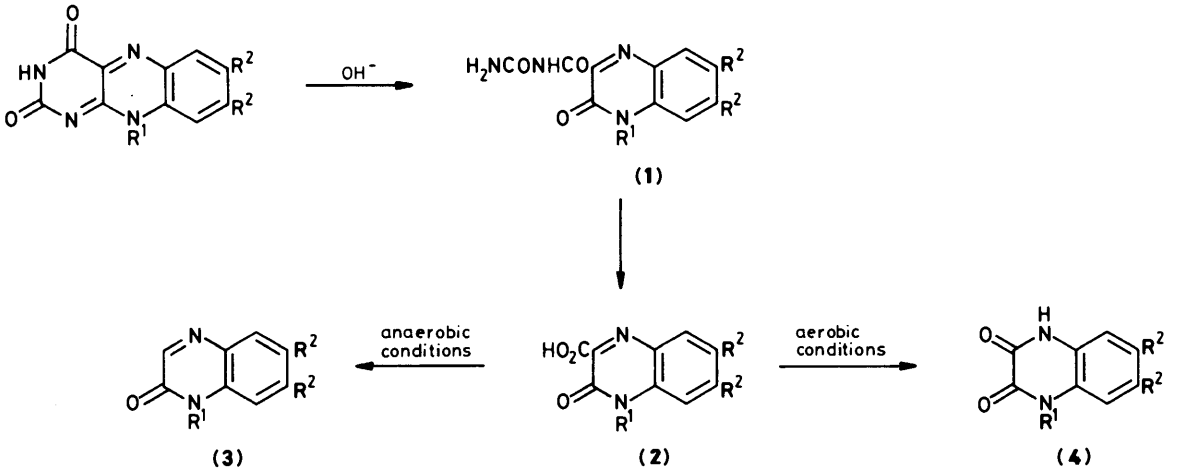
Hydrolysis of the flavin (**5**) with Triton B gave the 4a-spirohydantoin (**6**) as the major product together with, among other products, the imidazo[4,5-*b*]quinoxaline (**7**). Formation of such products indicates that nucleophilic attack by hydroxide ion on the flavin ring had occurred preferentially at the 10a-position.

For flavin cofactors, which are concerned with a variety of *in vivo* redox processes, kinetic studies have shown that some oxidations proceed *via* covalent addition of a substrate anion predominantly to the C-4a and N-5 positions of an isoalloxazine ring system.[1-8] For such studies, it was of importance to determine by chemical means which isoalloxazine position is most susceptible to nucleophilic attack. We therefore studied the hydrolysis of isoalloxazine (flavin) with hydroxide ion as a representative though hard nucleophile, in order to gain information concerning the position of nucleophilic addition; such studies were first investigated as early as 1932.[9] Previous studies have shown that riboflavin,[9,10] lumiflavin,[11,12] and 10-methylisoalloxazine[12,13] were hydrolysed *via* (**1**) and (**2**) to give the quinoxalinone (**3**) and/or the quinoxaolinedione (**4**) (see Scheme 1). In 1977, one of the present authors (F. Yoneda) investigated the hydrolysis of the isoalloxazines (**5a**—**e**) with Triton B in dimethylformamide (DMF) at room temperature in the dark and obtained the 4a-spirohydantions (**6a**—**e**) as the major products and the isoimidazolonequinoxalines (**7a**—**e**) as the minor products. In addition, hydrolysis of (**5a**) gave 1-phenylbenzimidazole (**8a**) and quinoxalinylidene(methyl)urea (**9a**). Hydrolysis of (**5c**) afforded methylaminoquinoxazolinone (**10c**) and hydrolysis of (**5d**) gave 3-methylalloxazine (**11**) and an unidentified compound (**A**), respectively.[16] Here we describe the details of these experiments.†

The molecular formula of the major product (**6a**—**e**) was in agreement with that corresponding to addition of a water molecule to the parent isoalloxazine (**5a**—**e**) (see Experimental section) whilst their ^{13}C n.m.r. spectra (see Table 1) showed the presence of three carbonyl carbons (δ *ca.* 164, 154, and 150) and

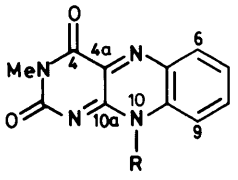


	R^1	R^2
Riboflavin	Ribityl	Me
Lumiflavin	Me	Me
10-Methylisoalloxazine	Me	H

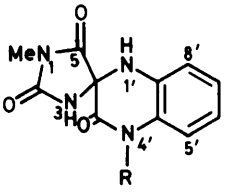
Scheme 1.

reported that hydrolysis of 10-alkylisoalloxazines (**5d**) and (**5e**) with benzyltrimethylammonium hydroxide (Triton B) gave the 4a-spirohydantoins (**6d**) and (**6e**); these structures which were presented tentatively, suggested that the 10a-position was susceptible to nucleophilic attack by hydroxide ion.[14] In contrast, Bruice *et al.* reported that hydrolysis of 10-arylisoalloxazine (**5a**) and (**5b**) afforded the imidazo[4,5-*b*]quinoxalines (**7a**) and (**7b**), initial hydroxide ion attack having occurred at the 4 position because of steric hindrance to attack at the 10a position arising from the presence of the 10-aryl group.[15] In order to provide a better understanding of these reactions, we have one quaternary sp^3 carbon (δ *ca.* 68) which seemed to indicate the presence of a spirohydantoin skeleton. As can be seen from

† In a preliminary communication,[16] we reported as a major product of the hydrolysis of (**5c**), an unidentified compound (**A**). An *X*-ray re-examination of this showed that it was the purine derivative (**B**) (see Figure 1), a by-product in the preparation of (**5c**); here we describe the result obtained by using pure (**5c**). Hydrolysis of (**5a**) under conditions similar to those reported by Bruice *et al.*[15] (methanolic KOH at room temp. for 26 h in the dark) gave (**6a**) (15.7%) and (**7a**) (1.5%) together with unchanged (**5a**) (62.2%).

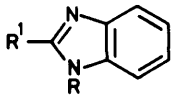


(5)



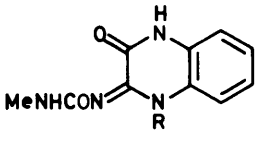
(6)

(7)

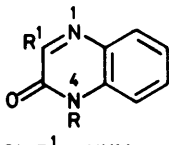


(8) R^1 = H

(17) R^1 = CONHMe

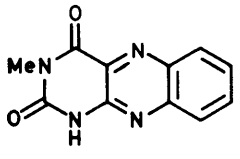


(9)



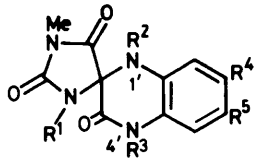
(10) R^1 = NHMe

(16) R^1 = CONHMe



(11)

a, R = Ph, b, R = 2′, 6′-$Me_2C_6H_3$, c, R = CH_2Ph, d, R = Me, e, R = Et



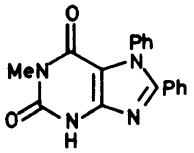
(12) R^1 = R^3 = R^4 = R^5 = Me, R^2 = H

(13) R^1 = H, R^2 = Et, R^3 = R^4 = R^5 = Me

(14) R^1 = H, R^3 = Et, R^2 = R^4 = R^5 = Me

(15) R^1 = R^5 = H, R^2 = $(CH_2)_2C_6H_4OMe$-*m*

R^3 = Et, R^4 = Br



(B)

Table 1. ^{13}C N.m.r. data for the skeletal carbons of the spirohydantoins (**6**) [in $(CD_3)_2SO$]

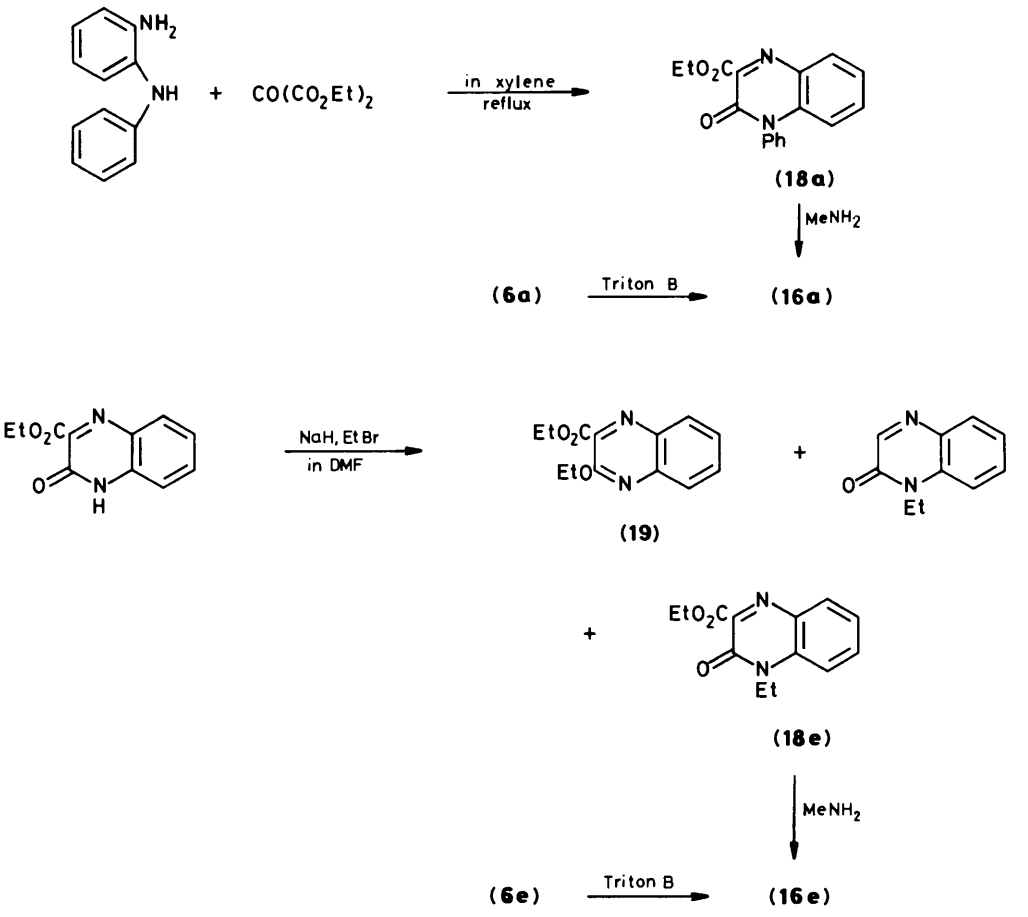
	(6a)	(6b)	(6c)	(6d)	(6e)
δ_C (p.p.m.)	164.2 (s)	164.6	164.7	164.6	164.6
	154.5 (s)	153.6	155.2	154.6	154.1
	150.0 (s)	150.0	149.9	149.9	149.9
	125.4 (s)	125.8	126.0	125.7	125.9
	121.4 (s)	119.1	118.9	119.9	118.5
	118.2 (d)	118.3	118.1	118.0	117.9
	112.9 (d)	113.0	112.9	113.0	113.1
	109.9 (d)	108.4	109.6	109.0	108.7
	108.5 (d)	108.3	108.2	107.9	108.4
	68.0 (s)	68.0	67.7	67.6	67.5

For δ_C which is not given in this Table, see the corresponding compound in the Experimental section.

Table 1, the similarity of the ^{13}C n.m.r. data suggests that, in contrast to the results by Bruice *et al.*,[15] the major products have a common skeleton regardless of the 10-substituent on the isoalloxazine (**5a**—**e**). 4a- and 10a-Spirohydantoin were expected products, being formed *via* an initial hydroxide ion attack on the 10a- and 4a-positions, respectively. In the ^1H n.m.r. spectra of the known spirohydantoins (**12**),[17] (**13**),[18] (**14**),[18] and (**15**),[19] derived from flavinium compounds (not flavins), (**12**) and (**13**) showed signals due to an 4′-NMe groups at δ 3.45 and 3.41, respectively, and (**14**) shows a signal due to 1′-Me group at δ 2.80. Further, (**13**) showed a signal due to the methylene protons of the 1′-NEt group at δ 3.08 and (**14**) and (**15**) showed signals due to the methylene protons of the 4′-NEt group at δ 4.01 and 4.07, respectively. As the ^1H n.m.r. spectra of the major products (**6d**) and (**6e**) showed a signal due to the N-Me group at δ 3.35 and the signal due to the methylene protons of N-Et group at δ 3.98, respectively, it seemed likely that these major products were the 4′-substituted 4a-spirohydantoins (**6a**—**e**). In order to confirm this, the main products (**6a**) and (**6e**) were treated with Triton B to provide in the case of the former quinoxaline-2-carboxamide (**16a**) and benzimidazole-2-carboxamide (**17a**), and in the case of the latter the quinoxaline-2-carboxamide (**16e**). The structures of these products were elucidated on the basis of spectral evidence. Thus, the i.r. spectra of (**16a**), (**16e**), and (**17a**) revealed NH absorption [(**16a**) 3 280, (**16e**) 3 300, and (**17a**) 3 420 cm^{-1}] and amide I and II bands [(**16a**) 1 682 and 1 540, (**16e**) 1 682 and 1 547, and (**17a**) 1 680 and 1 545 cm^{-1}]. In addition, each ^1H n.m.r. spectra showed a 3 H doublet at δ *ca.* 3.00, which collapsed to a singlet, the NH signal also disappeared on addition of deuterium oxide; these results suggested the presence of a MeNHCO group. From these results and evidence of molecular composition based upon the accurate mass spectrum (see Experimental section), the structures of (**16a**), (**16e**), and (**17a**) were deduced; those of the first two were confirmed by comparison with authentic samples prepared by the routes depicted in Scheme 2.

Whereas treatment of (**16a**) with Triton B in DMF resulted in the formation of (**17a**), (**16e**) gave a complex mixture, results which indicate that the major hydrolysis product of isoalloxazine (**5a**—**e**) was the 4a-spirohydantoin (**6a**—**e**). This assumption was finally confirmed by an *X*-ray analysis of (**6a**)·$(CD_3)_2SO$ solvate (see Figure 2). The structures of the minor products (**7a**), (**7c**), and (**7e**) were elucidated by comparison of these data with those of (**7b**) reported by Bruice *et al.*[15] (see Table 2).

Among other by-products, compound (**8a**) was identified on the basis of its molecular weight (by mass spectrometry) and spectral evidence, *i.e.* absence of an NMe signal in its ^1H n.m.r. spectrum and absence of carbonyl absorption in its i.r. spectrum. The structure of compound (**9a**) was elucidated on the basis (i) its i.r. spectrum showed NH absorption (3 350 cm^{-1}) and amide I and II bands (1 710 and 1 490 cm^{-1}), (ii) that its ^1H n.m.r. spectrum showed signals due to an MeNH group [δ 2.85 (3 H, d, *J* 4.7 Hz, MeN) and 9.59 (1 H, br s, NH)], and (iii) from its molecular composition. Thus compound (**9a**) corresponds to



Scheme 2.

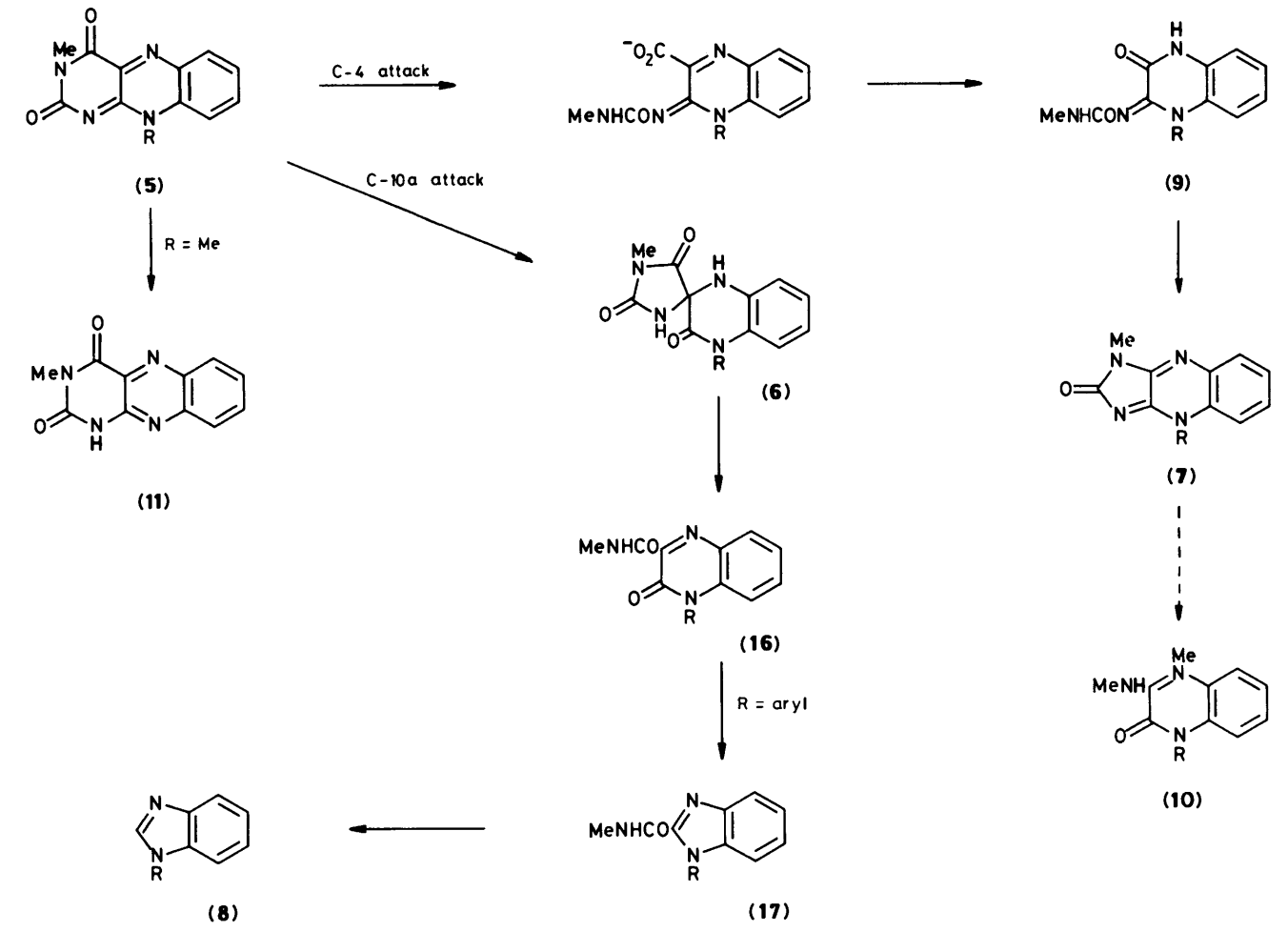
Table 2. I.r. (in $CHCl_3$) and ^1H n.m.r. (200 MHz in $CDCl_3$) data for the imidazo[4,5-*b*]quinoxalinones (**7**)

	(**7a**)	(**7b**)	(**7c**)	(**7e**)	*cf.* (**7b**)[a]
$\nu_{max.}$	1 730 1 660 1 610 1 585 1 560 1 490	1 725 1 660 1 605 1 585 1 565 1 493	1 722 1 660 1 600 1 560 1 496	1 725 1 660 1 600 1 560 1 500	1 720
δ_H N-Me	3.53 (s)	3.54 (s)	3.53 (s)	3.44 (s)	3.51 (s)
5-H	7.97 (dd, *J* 7.2, 1.4 Hz)	7.99 (dd, *J* 8.2, 1.5 Hz)	7.92 (m)	7.88 (dd, *J* 7.7, 1.7 Hz)	
6-H	7.36 (ddd, *J* 7.2, 7.2, 1.4 Hz)	7.35 (ddd, *J* 8.2, 8.2, 1.5 Hz)	7.42—7.58 (3 H, m, ArH)	7.48 (ddd, *J* 7.7, 7.7, 1.7 Hz)	6.8—8.1 (7 H, m, ArH)
7-H	7.49 (ddd, *J* 7.2, 7.2, 1.4 Hz)	7.50 (ddd, *J* 8.2, 8.2, 1.5 Hz)		7.55 (ddd, *J* 7.7, 7.7, 1.7 Hz)	
8-H	7.09 (dd, *J* 7.2, 1.4 Hz)	6.89 (dd, *J* 8.2, 1.5 Hz)		7.62 (dd, *J* 7.7, 1.7 Hz)	
Others	7.41—7.68 (5 H, m, ArH)	1.95 (6 H, s, Me) 7.26—7.41 (3 H, m, ArH)	5.80 (2 H, s, CH_2) 7.26—7.39 (5 H, m, ArH)	1.53 (3 H, t, *J* 7.2 Hz, Me) 4.63 (2 H, q, *J* 7.2 Hz, CH_2)	1.97 (6 H, s, Me)

[a] Ref. 15.

the hypothetical intermediate proposed by Bruice *et al.* in kinetic work on the hydrolysis of isoalloxazine (**5b**) to give the imidazo[4,5-*b*]quinoxalinone (**5b**).[15] The structure of compound (**10c**) was elucidated on the basis of MeNH n.m.r. signals [δ 3.17 (3 H, d, *J* 2.9 Hz, Me-N), and 6.47 (1 H, br s, NH)] and its molecular composition by an accurate mass spectrometric measurement. The structure of the compound (**11**) was presumed on the basis of spectral evidence (see Experimental section and Scheme 3). Thus, hydroxide ion attack on the 10a-position of the isoalloxazine (**5**) produces the quinoxalinecarboxamide (**16**) *via* the 4a-spirohydantoin (**6**). When (**16**) has a 4-aryl substituent it would be further hydrolysed to give the benzimidazole (**8**) *via* the benzimidazolecarboxamide (**17**). On the other hand, hydroxide ion attack on the 4-position of the isoalloxazine (**5**) produces imidazo[4,5-*b*]quinoxalinone (**7**) *via* compound (**9**). Since methylaminoquinoxalinone (**10**) was not isolated in further hydrolysis of spirohydantoin (**6**) with Triton B, (**10**) was presumably produced by the hydrolysis of (**7**).

As can be seen from the summarising results of hydrolysis in Table 3 the hydroxide ion attacks the 10a-position in preference to the 4-position. Consequently, such steric hindrance by the 10-aryl substituent at the 10a-position as reported by Bruice *et al.* was not observed. This fact is understandable by assuming that the 10-aryl group is lying perpendicularly to the plane of the isoalloxazine ring, so that the steric influence of the aryl group on the 10a-position is small. This assumption is supported by the ^1H n.m.r. spectral data, that is, the highfield shift of the 9-H signal of 10-arylisoalloxazine [(**5a**) δ 6.90; (**5b**) δ 6.78] in comparison with that of 10-alkylisoalloxazine [(**5d**) δ 7.67 (**5e**)



Scheme 3.

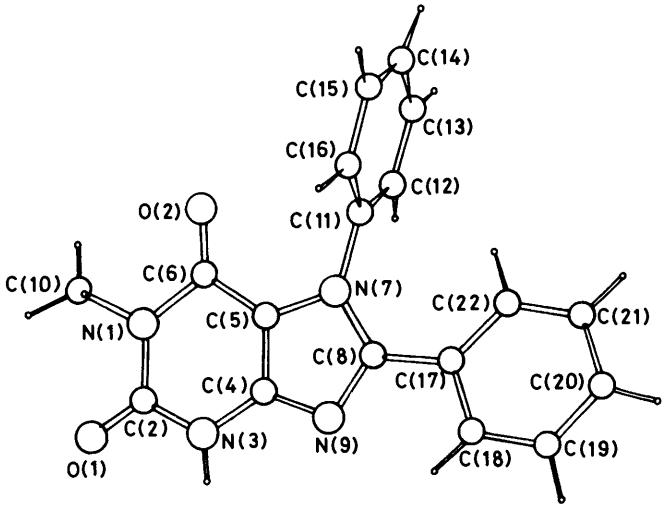


Figure 1. Molecular structure of the purine derivative (**B**)

δ 7.69]. The similar highfield shifts are still observed in the spirohydantoin (**6a,b**) and imidazoquinoxalinone (**7a,b**). In conclusion, hydroxide ion attack on the isoalloxazine ring takes place mainly at the 10a-position regardless of the 10-substituent.

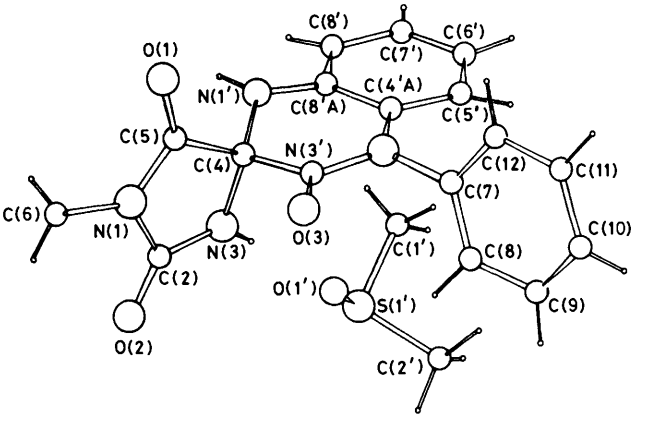


Figure 2. Molecular structure of the spirohydantoin (**6a**)·DMSO-d_6 solvate

Therefore, on considering reactions related to the flavin cofactor, the 10a-adduct of the substrate anion as well as the 4a- or 5-adduct should be taken into account.

Experimental

M.p.s were taken on a Yanagimoto micro melting point apparatus and are uncorrected. I.r. spectra were obtained on a

Table 3. Results (%) of hydrolysis of the isoalloxazines (**5**)

Isoalloxazine	(**5a**)	(**5b**)	(**5c**)	(**5d**)	(**5e**)
Spirohydantoin (**6**)	76.5	54.4	37.7	3.4	55.6
Imidazo[4,5-*b*]-quinoxaline (**7**)	3.9	16.4	14.9		36.6
Others	(**8**) 5.5		(**10**) 15.1	(11) 20.6	
	(**9**) 4.8			(**A**) 16.6	
C-10a attack	81.1	54.4	37.7	3.4	55.6
C-4 attack	8.7	16.4	30.0		36.6

Table 4. Atomic parameters for non-hydrogen atoms in purine derivative (**B**). Estimated standard deviations are given in parentheses.

Atom	*x*	*y*	*z*
N(1)	0.228 8(1)	0.581 0(1)	0.651 1(2)
C(2)	0.343 0(2)	0.551 9(2)	0.608 1(3)
N(3)	0.450 6(1)	0.664 6(1)	0.632 5(2)
C(4)	0.443 2(2)	0.798 3(2)	0.682 1(2)
C(5)	0.330 0(2)	0.824 0(2)	0.714 6(2)
C(6)	0.211 4(2)	0.715 0(2)	0.702 8(3)
N(7)	0.359 4(1)	0.969 4(1)	0.762 1(2)
C(8)	0.488 4(2)	1.021 4(2)	0.755 0(2)
N(9)	0.542 2(1)	0.917 9(1)	0.705 8(2)
C(10)	0.115 9(2)	0.459 4(2)	0.639 0(5)
C(11)	0.265 3(2)	1.042 9(2)	0.812 9(2)
C(12)	0.204 5(2)	1.052 8(2)	0.663 6(3)
C(13)	0.110 3(2)	1.117 3(2)	0.711 9(4)
C(14)	0.078 3(2)	1.168 0(2)	0.903 5(4)
C(15)	0.140 0(2)	1.159 0(2)	1.050 3(4)
C(16)	0.235 8(2)	1.096 6(2)	1.005 7(3)
C(17)	0.567 2(2)	1.169 6(2)	0.794 3(2)
C(18)	0.697 7(2)	1.200 2(2)	0.816 2(3)
C(19)	0.779 2(2)	1.335 1(2)	0.846 3(3)
C(20)	0.733 2(2)	1.442 7(2)	0.855 4(3)
C(21)	0.604 9(2)	1.414 8(2)	0.837 2(3)
C(22)	0.521 7(2)	1.279 9(2)	0.805 2(3)
O(1)	0.345 7(1)	0.430 3(1)	0.553 3(3)
O(2)	0.106 1(1)	0.727 6(1)	0.733 3(2)

Table 5. Bond lengths (Å) and valence angles (°) in purine derivative (**B**)

Bond	Length	Bond	Length
N(1)–C(2)	1.388(3)	N(1)–C(6)	1.413(3)
N(1)–C(10)	1.462(2)	C(2)–N(3)	1.363(2)
C(2)–O(1)	1.222(2)	N(3)–C(4)	1.366(2)
C(4)–C(5)	1.358(3)	C(4)–N(9)	1.353(2)
C(5)–C(6)	1.431(3)	C(5)–N(7)	1.389(2)
C(6)–O(2)	1.215(3)	N(7)–C(8)	1.365(2)
N(7)–C(11)	1.450(3)	C(8)–N(9)	1.345(3)
C(8)–C(17)	1.471(3)	C(11)–C(12)	1.380(3)
C(11)–C(16)	1.366(2)	C(12)–C(13)	1.387(3)
C(13)–C(14)	1.362(4)	C(14)–C(15)	1.366(4)
C(15)–C(16)	1.389(3)	C(17)–C(18)	1.396(3)
C(17)–C(22)	1.395(4)	C(18)–C(19)	1.377(3)
C(19)–C(20)	1.375(4)	C(20)–C(21)	1.373(3)
C(21)–C(22)	1.381(3)		

Bond	Angle	Bond	Angle
C(2)–N(1)–C(6)	126.5(1)	C(2)–N(1)–C(10)	115.9(1)
C(6)–N(1)–C(10)	117.5(1)	N(1)–C(2)–N(3)	117.0(2)
N(1)–C(2)–O(1)	120.8(2)	N(3)–C(2)–O(1)	122.2(2)
C(2)–N(3)–C(4)	120.4(2)	N(3)–C(4)–C(5)	121.6(2)
N(3)–C(4)–N(9)	126.1(2)	C(5)–C(4)–N(9)	112.3(2)
C(4)–C(5)–C(6)	122.9(2)	C(4)–C(5)–N(7)	105.4(2)
C(6)–C(5)–N(7)	131.6(2)	N(1)–C(6)–C(5)	111.3(2)
N(1)–C(6)–O(2)	120.9(2)	C(5)–C(6)–O(2)	127.8(2)
C(5)–N(7)–C(8)	106.2(2)	C(5)–N(7)–C(11)	123.7(1)
C(8)–N(7)–C(11)	130.0(1)	N(7)–C(8)–N(9)	111.7(1)
N(7)–C(8)–C(17)	127.8(2)	N(9)–C(8)–C(17)	120.6(2)
C(4)–N(9)–C(8)	104.4(2)	N(7)–C(11)–C(12)	118.8(1)
N(7)–C(11)–C(16)	119.6(2)	C(12)–C(11)–C(16)	121.5(2)
C(11)–C(12)–C(13)	118.8(2)	C(12)–C(13)–C(14)	120.0(3)
C(13)–C(14)–C(15)	120.7(2)	C(14)–C(15)–C(16)	120.3(2)
C(11)–C(16)–C(15)	118.7(2)	C(8)–C(17)–C(18)	117.0(2)
C(8)–C(17)–C(22)	124.9(2)	C(18)–C(17)–C(22)	118.1(2)
C(17)–C(18)–C(19)	121.0(2)	C(18)–C(19)–C(20)	120.4(2)
C(19)–C(20)–C(21)	119.4(2)	C(20)–C(21)–C(22)	121.1(2)
C(17)–C(22)–C(21)	120.1(2)		

Shimadzu IR-400 spectrometer and ^{1}H n.m.r. spectra on a JEOL FX 200 or JEOL PMX-60 spectrometer. ^{13}C N.m.r. (50.10 MHz) spectra were recorded on the JEOL FX 200 spectrometer. The n.m.r. data are reported relative to internal tetramethylsilane. Mass spectra were taken on a JEOL JMS 01SG-2 instrument by direct insertion at 70 eV. Column chromatography was carried out with Silica gel 60 (E. M. Merck, 70—230 mesh) and preparative t.l.c. was run on 20 × 20 cm plates coated with a 0.25—0.5 mm layer of Merck silica gel GF 254 or PF 254. Benzyltrimethylammonium hydroxide (Triton B) was purchased from Tokyo Kasei Kogyo Co. Ltd. as a 40% methanolic solution.

Preparation of Isoalloxazines

(a) 10-(2′,6′-*Dimethylphenyl*)-3-*methylisoalloxazine* (**5b**).—6-Chloro-3-methyluracil[20] (3.27 g, 20.0 mmol) was suspended in 2,6-dimethylaniline (7.4 ml, 60.0 mmol) and the mixture stirred at 160—170 °C for 1.5 h. The purple reaction mixture was then diluted with ether and triturated. The resulting precipitate was filtered off and recrystallised from ethanol to give 6-(2′,6′-*dimethylphenyl*)-3-*methyluracil* as colourless needles (2.54 g, 50.9%), m.p. 275—278 °C; $\nu_{max.}$(Nujol) 3 250 (NH), 1 710 and 1 695 (CO), 1 640, and 1 590br cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 2.17 (6 H, s, 2′- and 6′-Me), and 3.04 (3 H, s, NMe), 3.85 (1 H, s, 5-H), 7.17 (3 H, s, 3′-, 4′-, and 5′-H), 7.64 (1 H, s, NH), and 10.63 (1 H, s, NH) (Found: *m/z* 245.1165. $C_{13}H_{15}N_3O_2$ requires *M*, 245.1164).

3-Methyl-6-(2′,6′-dimethylphenyl)uracil (1.94 g, 7.92 mmol) and nitrosobenzene (2.54 g, 23.7 mmol) were dissolved in a mixture of acetic acid (3.2 ml) and acetic anhydride (12.8 ml) and the solution was stirred under reflux for 2.5 h. The reaction mixture was concentrated under reduced pressure, diluted with ethanol, and cooled. The precipitate was filtered off and recrystallised from ethanol to give 6-(2′,6′-dimethylphenyl)-3-methylisoalloxazine (**5b**) as yellow needles (1.60 g, 60.9%), m.p. > 300 °C (lit.,[21] 298—300 °C).

(b) 10-*Benzyl*-3-*methylisoalloxazine* (**5c**). The title compound was prepared by the literature method[22] but the solid obtained was a mixture of isoalloxazine (**5c**) and 1-*methyl*-7,8-*diphenylpurine*-2,6(1H,3H)-*dione* (**B**). This mixture was dissolved in CH_2Cl_2 and chromatographed. The fraction eluted with ether was recrystallised from $CHCl_3$–methanol to give the dione (**B**), as colourless plates (439.4 mg, 13.7%), m.p. > 300 °C (Found: C, 67.7; H, 4.4; N, 17.6%; M^+, 318. $C_{18}H_{14}N_4O_2$ requires C, 67.9; H, 4.4; N, 17.6%; *M*, 318); $\nu_{max.}$(Nujol) 1 705 and 1 645 cm^{-1} (CO); δ_H [200 MHz; $(CD_3)_2SO$] 3.15 (3 H, s, N-Me), 7.36 (5 H, m, ArH), and 7.39—7.50 (5 H, m, ArH). Elution with CH_2Cl_2–ether (1:1) afforded the isoalloxazine (**5c**) as yellow needles (616.2 mg, 19.2%), m.p. 296 °C (from MeOH–$CHCl_3$) (lit.,[22] 284 °C).

3-Methyl-10-phenylisoalloxazine (**5a**),[22] 3,10-dimethylisoalloxazine (**5d**),[22] and 10-ethyl-3-methylisoalloxazine (**5e**),[23] were prepared by literature methods.

Hydrolysis of the Isoalloxazine (**5a**).—A mixture of the isoalloxazine (**5a**) (1.09 g, 3.59 mmol) and Triton B (3.02 g,

Table 6. Atomic parameters for non-hydrogen atoms in spirohydantoin (**6a**)·$(CD_3)_2SO$ solvate. Estimated standard deviations are given in parentheses

Atom	*x*	*y*	*z*
N(1)	0.376 4(3)	0.021 1(4)	1.003 2(5)
C(2)	0.439 2(4)	0.105 6(5)	1.040 6(6)
N(3)	0.459 1(3)	0.158 2(4)	0.935 0(4)
C(4)	0.406 6(3)	0.123 8(5)	0.824 6(5)
C(5)	0.356 5(4)	0.021 1(5)	0.878 1(6)
N(1′)	0.443 5(3)	0.079 5(4)	0.720 5(4)
C(3′)	0.350 9(4)	0.234 4(5)	0.788 2(5)
N(4′)	0.367 0(3)	0.304 3(4)	0.688 4(4)
C(4′A)	0.428 3(3)	0.275 0(5)	0.613 4(5)
C(5′)	0.446 7(4)	0.352 9(6)	0.518 3(6)
C(6′)	0.506 7(4)	0.319 7(7)	0.445 2(6)
C(7′)	0.548 9(4)	0.210 2(6)	0.467 9(6)
C(8′)	0.530 1(4)	0.132 1(6)	0.563 7(6)
C(8′A)	0.468 2(3)	0.161 8(5)	0.635 1(5)
C(6)	0.339 9(5)	−0.059 2(7)	1.090 0(7)
C(7)	0.325 8(4)	0.423 1(6)	0.672 3(6)
C(8)	0.353 9(4)	0.519 6(6)	0.752 4(6)
C(9)	0.312 0(6)	0.632 7(6)	0.738 3(8)
C(10)	0.247 6(6)	0.646 0(8)	0.648 4(9)
C(11)	0.222 3(5)	0.550 1(8)	0.569 1(9)
C(12)	0.261 4(4)	0.436 9(7)	0.581 3(7)
O(1)	0.308 1(3)	−0.044 6(4)	0.818 0(5)
O(2)	0.468 1(3)	0.122 3(4)	1.149 0(4)
O(3)	0.297 6(3)	0.258 4(4)	0.852 5(4)
S(1′)	0.624 0(1)	0.422 3(2)	0.891 2(2)
C(1′)	0.638 4(4)	0.395 6(7)	0.732 0(7)
C(2′)	0.612 3(5)	0.585 6(7)	0.887 0(8)
O(1′)	0.540 9(4)	0.372 5(5)	0.904 4(6)

7.22 mmol) in dimethylformamide (DMF) (9 ml) was stirred at room temperature for 25 h in the dark. The reaction mixture was neutralised with acetic acid and evaporated to dryness under reduced pressure. The residue was taken up in a little methanol and chromatographed. The fraction eluted with ether–hexane (3:7) was further separated by preparative t.l.c. [methanol–$CHCl_3$ (6:94)]. The less polar zone afforded 1-(3-*oxo*-1-*phenylquinoxalin*-2-*ylidene*)-3-*methylurea* (**9a**) as colourless needles (51.0 mg, 4.8%), m.p. 210—212 °C (from ether–$CHCl_3$) (Found: C, 65.1; H, 4.7; N, 19.3. $C_{16}H_{14}N_4O_2$ requires C, 65.3; H, 4.8; N, 19.0%); $\nu_{max.}$($CHCl_3$) 3 350 (NH) 1 710 (amide I band), and 1 490 cm^{-1} (amide II band); δ_H (200 MHz; $CDCl_3$) 2.85 (3 H, d, *J* 4.7 Hz, collapsed to singlet by adding D_2O, NH-*Me*), 7.15 (1 H, m, 8′-H), 7.32—7.45 (4 H, m, Ar*H*), 7.54—7.62 (3 H, m, Ar*H*), 7.87 (1 H, m, 5′-H), 7.91 (1 H, br s, NH), and 9.59 (1 H, br s, NH). The middle zone afforded 1-phenylbenzimidazole (**8a**)[24] (38.2 mg, 5.5%); $\nu_{max.}$($CHCl_3$) 1 600, 1 500, and 1 455 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 7.29—7.36 (3 H, m, 5-, 6-, and 7-H), 7.41—7.60 (5 H, m, ArH), 7.88 (1 H, m, 4-H), and 8.12 (1 H, s, 2-H); *m/z* 194 (M^+). The most polar zone gave 1-*methyl*-4-*phenylimidazo*[4,5-b]*quinoxalin*-2(4H)-*one* (**7a**) as colourless needles (38.9 mg, 3.9%), m.p. >296 °C (from MeOH) (Found: C, 69.3; H, 4.2; N, 20.3%; M^+, 276. $C_{16}H_{12}N_4O$ requires C, 69.55; H, 4.4; N, 20.3%; *M*, 276); $\nu_{max.}$ and δ_H, see Table 2. The fraction eluted with ether–hexane (1:1) was recrystallised from $CHCl_3$ to give 1-*methyl*-4′-*phenylspiro*-[*imidazolidine*-4,2′(1′H)-3′,4′-*dihydroquinoxaline*]-2,3′,5-*trione* (**6a**) as colourless needles (873 mg, 75.6%), m.p. 227 °C (Found: C, 63.4; H, 4.3; N, 17.35%; M^+, 322. $C_{17}H_{14}N_4O_3$ requires C, 63.35; H, 4.4; N, 17.4%; *M*, 322); $\nu_{max.}$(Nujol) 3 350 and 3 270 (NH), 1 770, 1 725, 1 710, and 1 690 (CO), 1 609, and 1 592 cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 2.92 (3 H, s, N-Me), 6.13 (1 H, d, *J* 7.6 Hz, 5′-H), 6.66 (1 H, dd, *J* 7.6 and 7.6 Hz, 7′-H), 6.85 (1 H, d, *J* 7.6 Hz, 8′-H), 6.95 (1 H, dd, *J* 7.6 and 7.6 Hz, 6′-H), 7.25—7.63 (5 H, m, ArH), and 9.44 (1 H, s, NH); δ_C 130.7 (s), 124.3 (2 × d), 123.1 (d), 122.9 (2 × d), 18.6 (q), and see Table 1. Concentration of a solution of (**6a**) in $(CD_3)_2SO$ under reduced pressure afforded a crystalline mass which was washed with hexane to give (**6a**)·$(CD_3)_2SO$ solvate as colourless plates, m.p. >298 °C (Found: C, 55.9; H, 6.15; N, 13.7; S, 8.1. $C_{19}H_{14}D_6N_4O_4S$ requires C, 56.1; H, 6.4; N, 13.8; S, 7.9%).

Table 7. Bond lengths (Å) and valence angles (°) in spirohydantoin (**6a**)·$(CD_3)_2SO$ solvate

Bond	Length	Bond	Length
N(1)–C(2)	1.419(8)	N(1)–C(5)	1.344(8)
N(1)–C(6)	1.459(10)	C(2)–N(3)	1.344(8)
C(2)–O(2)	1.220(7)	N(3)–C(4)	1.441(7)
C(4)–C(5)	1.544(8)	C(4)–N(1′)	1.422(7)
C(4)–C(3′)	1.541(8)	C(5)–O(1)	1.209(8)
N(1′)–C(8′A)	1.375(7)	C(3′)–N(4′)	1.362(7)
C(3′)–O(3)	1.222(8)	N(4′)–C(4′A)	1.416(7)
N(4′)–C(7)	1.460(8)	C(4′A)–C(5′)	1.385(9)
C(4′A)–C(8′A)	1.402(7)	C(5′)–C(6′)	1.396(10)
C(6′)–C(7′)	1.387(10)	C(7′)–C(8′)	1.394(9)
C(8′)–C(8′A)	1.401(9)	C(7)–C(8)	1.398(9)
C(7)–C(12)	1.380(9)	C(8)–C(9)	1.411(10)
C(9)–C(10)	1.372(13)	C(10)–C(11)	1.376(13)
C(11)–C(12)	1.388(11)	S(1′)–C(1′)	1.775(8)
S(1′)–C(2′)	1.776(8)	S(1′)–O(1′)	1.522(7)

Bond	Angle	Bond	Angle
C(2)–N(1)–C(5)	111.9(5)	C(2)–N(1)–C(6)	123.9(5)
C(5)–N(1)–C(6)	124.2(5)	N(1)–C(2)–N(3)	106.6(5)
N(1)–C(2)–O(2)	124.5(6)	N(3)–C(2)–O(2)	129.0(6)
C(2)–N(3)–C(4)	113.2(5)	N(3)–C(4)–C(5)	100.9(4)
N(3)–C(4)–N(1′)	116.7(4)	N(3)–C(4)–C(3′)	107.8(4)
C(5)–C(4)–N(1′)	110.9(5)	C(5)–C(4)–C(3′)	108.0(5)
N(1′)–C(4)–C(3′)	111.8(4)	N(1)–C(5)–C(4)	106.7(5)
N(1)–C(5)–O(1)	127.3(6)	C(4)–C(5)–O(1)	126.0(6)
C(4)–N(1′)–C(8′A)	119.9(4)	C(4)–C(3′)–N(4′)	117.2(5)
C(4)–C(3′)–O(3)	119.2(5)	N(4′)–C(3′)–O(3)	123.5(5)
C(3′)–N(4′)–C(4′A)	123.1(5)	C(3′)–N(4′)–C(7)	116.4(5)
C(4′A)–N(4′)–C(7)	119.8(5)	N(4′)–C(4′A)–C(5′)	121.5(5)
N(4′)–C(4′A)–C(8′A)	117.9(5)	C(5′)–C(4′A)–C(8′A)	120.6(5)
C(4′A)–C(5′)–C(6′)	119.7(6)	C(5′)–C(6′)–C(7′)	120.7(6)
C(6′)–C(7′)–C(8′)	119.3(6)	C(7′)–C(8′)–C(8′A)	120.8(6)
N(1′)–C(8′A)–C(4′A)	119.9(5)	N(1′)–C(8′A)–C(8′)	121.2(5)
C(4′A)–C(8′A)–C(8′)	118.8(5)	N(4′)–C(7)–C(8)	117.5(5)
N(4′)–C(7)–C(12)	120.2(6)	C(8)–C(7)–C(12)	122.4(6)
C(7)–C(8)–C(9)	116.8(6)	C(8)–C(9)–C(10)	120.7(7)
C(9)–C(10)–C(11)	121.2(8)	C(10)–C(11)–C(12)	119.7(8)
C(7)–C(12)–C(11)	119.1(7)	C(1′)–S(1′)–C(2′)	99.5(4)
C(1′)–S(1′)–O(1′)	105.2(3)	C(2′)–S(1′)–O(1′)	104.7(4)

Hydrolysis of the Isoalloxazine (**5b**).—A mixture of the isoalloxazine (**5b**) (54.1 mg, 0.16 mmol) and Triton B (103.4 mg, 0.25 mmol) in DMF (1 ml) was stirred at room temperature for 9 h in the dark. The reaction mixture was neutralised with acetic acid and evaporated to dryness. The residue was taken up in a little of methanol and chromatographed. Elution with ether–hexane (3:7) afforded 9-(2′,6′-dimethylphenyl)-3-methylimidazo[4,5-*b*]quinoxalin-2(3*H*)-one (**7b**)[15] (8.4 mg, 16.4%); $\nu_{max.}$ and δ_H, see Table 2 (Found: *m/z* 304.1325. $C_{18}H_{16}N_4O$ requires *M*, 304.1324). The eluate with ether–hexane (1:1) was recrystallised from $CHCl_3$ to give 1-*methyl*-4′-(2″,6″-*dimethylphenyl*)*spiro*[*imidazolidine*-4,2′(1′H)-3′,4′-*dihydroquinoxaline*]-2,3′,5-*trione* (**6b**) colourless needles (31 mg, 54.4%), m.p. 253—255 °C; $\nu_{max.}$(Nujol) 3 300 (NH), 1 775, 1 725, 1 715, and 1 685 (CO) cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 1.92, 2.03 (each 3 H, s, 2″- and 6″-Me), 2.91 (3 H, s, N-Me), 5.98 (1 H, d, *J* 7.6 Hz, 5′-H), 6.63 (1 H, dd, *J* 7.6 and 7.6 Hz, 7′-H), 7.20—7.40 (3 H, m, 3″-, 4″-, and 5″-H), 7.63 (1 H, s, NH), and 9.50 (1 H, s, NH); δ_C 130.2,

129.9, 128.3, 123.0, 122.9, 122.8, 18.4, 11.1, 10.8, and see Table 1 (Found: *m/z* 350.1379. $C_{19}H_{18}N_4O_3$ requires *M*, 350.1379).

Hydrolysis of the Isoalloxazine (**5c**).—A mixture of the isoalloxazine (**5c**) (171.9 mg, 0.54 mmol) and Triton B (460 mg, 1.10 mmol) in DMF (1.8 ml) was stirred at room temperature for 24 h in the dark. The reaction mixture was neutralised with acetic acid and evaporated to dryness. The residue was triturated with methanol and the precipitate was collected. Recrystallisation from methanol afforded 4′-*benzyl*-1-*methylspiro*[*imidazolidine*-4,2′(1′H)-3′,4′-*dihydroquinoxaline*]-2,3′-5-*trione* (**6c**) as colourless needles (17 mg, 9.4%), m.p. 246—249 °C; $\nu_{max.}$(Nujol) 3 300 and 3 225 (NH), 1 780, 1 735, and 1 650 (CO), and 1 600 cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 2.92 (3 H, s, N-Me), 5.21 (2 H, s, CH_2), 6.70 (1 H, dd, *J* 7.5 and 7.5 Hz, 7′-H), 6.78 (1 H, d, *J* 7.5 Hz, 5′-H), 6.91 (1 H, d, *J* 7.5 Hz, 8′-H), 6.93 (1 H, dd, *J* 7.5 and 7.5 Hz, 6′-H), 7.25—7.35 (5 H, m, ArH), 7.56 (1 H, s, NH), and 9.43 (1 H, s, NH); δ_C 130.2, 122.8, 121.3, 120.5, 39.0, 18.5, and see Table 1 (Found: *m/z* 336.1214. $C_{18}H_{16}N_4O_3$ requires *M*, 336.1223). The mother liquors were combined, evaporated to dryness, and chromatographed. Elution with ether–hexane (3:7) afforded 1-*benzyl*-3-*methylaminoquinoxaline*-2(3H)-*one* (**10c**) as colourless needles (21.7 mg, 15.1%), m.p. 175—177 °C (from $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 420 (NH), 1 650 (CO), 1 615, and 1 590 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 3.17 (3 H, d, *J* 2.9 Hz, collapsed to singlet upon addition of D_2O, NH-*Me*), 5.51 (2 H, s, CH_2), 6.47 (1 H, br s, NH), 7.11 (1 H, dd, *J* 6.0 and 1.3 Hz, 5-H), 7.16—7.36 (7 H, m, 6- and 7-H, and ArH), and 7.59 (1 H, d, *J* 8.1 Hz, 8-H) (Found: *m/z* 265.1220. $C_{16}H_{15}N_3O$ requires *M*, 265.1255). The eluate with ether–hexane (1:1) was subjected to preparative t.l.c. [methanol–$CHCl_3$ (3:97)]. The less polar zone afforded 4-*benzyl*-1-*methyl*-1H-*imidazo*[4,5-b]*quinoxalin*-2(4H)-*one* (**7c**) as pale yellow needles (23.3 mg, 14.9%), m.p. 286.5 °C (from MeOH); $\nu_{max.}$ and δ_H, see Table 2 (Found: *m/z* 290.1169. $C_{17}H_{14}N_4O$ requires *M*, 290.1168). The more polar zone afforded the additional spirohydantoin (**6c**). The total amount of spirohydantoin (**6c**) was 51.4 mg (28.3%).

Hydrolysis of the Isoalloxazine (**5d**).—A mixture of isoalloxazine (**5d**) (306.5 mg, 1.27 mmol) and Triton B (1.17 g, 2.80 mmol) in DMF (3 ml) was stirred at room temperature for 6.5 h in the dark. The reaction mixture was neutralised with acetic acid, diluted with water, and left overnight in a cold room. The precipitate was filtered off and recrystallised from acetic acid to give an unidentified compound (**A**) as colourless needles (61.1 mg), m.p. >300 °C; $\nu_{max.}$(Nujol) 3 140 (NH), 1 680—1 710 (CO), 1 650, 1 610, and 1 535 cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 3.18 (3 H, s) and 3.60 (1 H, s); *m/z* 291 and 277. The filtrate was evaporated to dryness and the residue was triturated with water. The precipitate was filtered off and recrystallised from methanol to afford 1,4′-*dimethylspiro*[*imidazolidine*-4,2′(1′H)-3′,4′-*dihydroquinoxaline*]-2,3′,5-*trione* (**6d**) as colourless needles, m.p. 283—285 °C (lit.,[14] 294 °C); $\nu_{max.}$(Nujol) 3 300 and 3 200 (NH), 1 780, 1 720, and 1 640 (CO) cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 2.90 (3 H, s, 1-N-Me), 3.35 (3 H, s, 4′-N-Me), 6.77 (1 H, dd, *J* 7.7 and 1.6 Hz, 5′-H), 6.84 (1 H, ddd, *J* 7.7, 7.7, and 1.6 Hz, 7′-H), 6.97 (1 H, ddd, *J* 7.7, 7.7, and 1.3 Hz, 6′-H), 7.11 (1 H, dd, *J* 7.7 and 1.3 Hz, 8′-H), 7.46 (1 H, s, NH), and 9.22 (1 H, s, NH); δ_C 23.2, 18.9, and see Table 1 (Found: *m/z* 260.0919. $C_{12}H_{12}N_4O_3$ requires *M*, 260.0909). The mother liquor of compound (**A**) was concentrated under reduced pressure. The residue was triturated with methanol and the precipitate was collected. Recrystallisation from methanol afforded 3-methylalloxazine (**11**) as pale yellow needles (59.6 mg, 20.6%), m.p. 273—275 °C (lit.,[25] m.p. 256—258 °C); $\nu_{max.}$(Nujol) 3 140 and 3 030 (NH), 1 740 and 1 680 (CO), 1 620, and 1 587 cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 3.32 (3 H, s, N-Me), 7.78 (1 H, dt, *J* 3.9 and 7.8 Hz, 7-H), 7.94 (2 H, d, *J* 3.9 Hz, 8- and 9-H), and 8.20 (1 H, d, *J* 7.8 Hz, 6-H); *m/z* 288 (M^+). The mother liquors of (**6d**) and (**11**) were combined and concentrated. The residue was subjected to preparative t.l.c. [methanol–$CHCl_3$ (6:94)] to give the addition spirohydantoin (**6d**). The total amount of (**6d**) was 11.2 mg, (3.4%).

Hydrolysis of the Isoalloxazine (**5e**).—A mixture of isoalloxazine (**5e**) (294.6 mg, 1.15 mmol) and Triton B (1.02 g, 2.44 mmol) in DMF (5 ml) was stirred at room temperature for 9.5 h in the dark. The reaction mixture was neutralised with acetic acid, diluted with water, and left overnight in a cold room. The precipitated mass was filtered off and recrystallised from $CHCl_3$–methanol to give 4′-ethyl-1-methylspiro[imidazolidine-4,2′(1′*H*)-3′-4′-dihydroquinoxaline]-2,3′,5-trione (**6e**) as colourless needles, m.p. 241—243 °C (lit.,[14] 232 °C) (Found: C, 57.1; H, 5.1; N, 20.5%; M^+, 274. Calc. for $C_{13}H_{14}N_4O_3$: C, 56.9; H, 5.15; N, 20.4%; *M*, 274); $\nu_{max.}$(Nujol) 3 320 and 3 250 (NH), 1 787, 1 730, and 1 645 (CO), cm^{-1}; δ_H [200 MHz; $(CD_3)_2SO$] 1.15 (3 H, t, *J* 7.1 Hz, C-Me), 2.89 (3 H, s, N-Me), 3.96 and 3.98 (each 1 H, q, *J* 7.1 Hz, CH_2), 6.77 (1 H, dd, *J* 7.7 and 1.4 Hz, 5′-H), 6.83 (1 H, ddd, *J* 7.7, 7.7, and 1.4 Hz, 7′-H), 6.96 (1 H, ddd, *J* 7.7, 7.7, and 1.4 Hz, 6′-H), 7.13 (1 H, dd, *J* 7.7 and 1.4 Hz, 8′-H), 7.43 (1 H, s, NH), and 9.24 (1 H, s, NH); δ_C 30.9, 18.4, and 6.39 (see also Table 1). The filtrate was concentrated and the residue was subjected to preparative t.l.c. [methanol–$CHCl_3$ (4:96)]. From the upper zone, 4-*ethyl*-1-*methyl*-1H-*imidazo*[4,5-b]-*quinoxaline*-2(4H)-*one* (**7e**) was obtained as colourless needles (96 mg, 36.6%), m.p. 223—224 °C (from ether–$CHCl_3$) (Found: C, 63.1; H, 5.0; N, 24.3%; M^+, 228. $C_{12}H_{12}N_4O$ requires C, 63.1; H, 5.3; N, 24.55%; *M*, 228); $\nu_{max.}$ and δ_H, see Table 2. From the lower zone, the additional spirohydantoin (**6e**) was obtained. The total amount of (**6e**) was 175.3 mg (55.6%).

Hydrolysis of the Spirohydantoin (**6a**).—A mixture of the spirohydantoin (**6a**) (113.4 mg, 0.35 mmol) and Triton B (221 mg, 0.53 mmol) in DMF (3 ml) was stirred at 125 °C for 1 h. The reaction mixture was neutralised with acetic acid and evaporated to dryness. The residue was subjected to preparative t.l.c. [methanol–$CHCl_3$ (3:97)]. From the less polar zone, N-*methyl*-1-*phenylbenzimidazole*-2-*carboxamide* (**17a**) was obtained as colourless needles (4.2 mg, 4.8%), m.p. 161—164 °C (from ether–$CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 420 (NH), 1 680 (amide I band), 1 600, and 1 545 (amide II band) cm^{-1}; δ_H (200 MHz; $CDCl_3$) 2.95 (3 H, d, *J* 5.1 Hz, collapsed to a singlet on addition of D_2O, NH*Me*), 7.16 (1 H, dd, *J* 6.8 and 2.4 Hz, 7-H), 7.29—7.59 (7 H, m, ArH), 7.68 (1 H, br s, NH), and 7.83 (1 H, dd, *J* 6.8 and 2.4 Hz, 4-H); δ_C($CDCl_3$) 159.2 (s), 143.8 (s), 141.1 (s), 138.0 (s), 136.7 (s), 129.2 (2 × d), 128.9 (d), 127.3 (2 × d), 125.1 (d), 123.8 (d), 120.5 (d), 111.6 (d), and 25.9 (q) (Found: *m/z* 251.1054. $C_{15}H_{13}N_3O$ requires *M*, 251.1059). From the more polar zone, N-*methyl*-4-*phenyl*-3-*oxo*-3,4-*dihydroquinoxaline*-2-*carboxamide* (**16a**) was obtained as yellow prisms (65.2 mg, 66.4%), m.p. 249—251 °C (from ether–$CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 280 (NH), 1 682 (amide I band), 1 640, 1 600, and 1 540 cm^{-1} (amide II band); δ_H [200 MHz; $(CD_3)_2SO$] 3.02 (3 H, d, *J* 4.7 Hz, collapsed to singlet on addition of D_2O, NH-*Me*), 6.74 (1 H, d, *J* 7.8 Hz, 5-H), 7.29 (2 H, dd, *J* 7.6 and 1.8 Hz, 2′- and 6′-H), 7.44 (1 H, dd, *J* 7.8 and 7.8 Hz, 7-H), 7.52 (1 H, dd, *J* 7.8 and 7.8 Hz, 6-H), 7.59—7.68 (3 H, m, 3′-, 4′-, and 5′-H), 8.31 (1 H, d, *J* 7.8 Hz, 8-H), and 9.60 (1 H, s, NH); δ_C($CDCl_3$) 162.6, 155.1, 144.9, 135.1, 134.5, 132.9, 132.6, 132.1, 130.5, 130.0, 127.9, 125.1, 115.7, and 26.7 (Found: *m/z* 279.1006. $C_{16}H_{13}N_3O_2$ requires *M*, 279.1008).

Hydrolysis of the Quinoxalinecarboxamide (**16a**).—A mixture of the quinoxalinecarboxamide (**16a**) (42.5 mg, 0.15 mmol) and Triton B (97.8 mg, 0.23 mmol) in DMF (1.5 ml) was stirred at 120 °C for 1.5 h under argon atmosphere. The reaction mixture

was neutralised with acetic acid and evaporated to dryness. The residue was purified by preparative t.l.c. [methanol–$CHCl_3$ (2:98)] to give the benzimidazolecarboxamide (**17a**) (17.9 mg, 46.8%). The i.r. and ^1H n.m.r. were identical with those of (**17**) obtained by hydrolysis of the spirohydantoin (**6a**).

Hydrolysis of the Spirohydantoin (**6e**).—A mixture of the spirohydantoin (**6e**) (46.5 mg, 0.17 mmol) and Triton B (147.2 mg, 0.35 mmol) in DMF (1 ml) was stirred for 1 h at 130 °C under an argon atmosphere. The reaction mixture was neutralised with acetic acid and evaporated to dryness. The residue was purified by preparative t.l.c. [methanol–$CHCl_3$ (5:95)] to give N-*methyl*-4-*ethyl*-3-*oxo*-3,4-*dihydroquinoline*-2-*carboxamide* (**16e**) as yellow needles (31.7 mg, 80.9%), m.p. 156—158 °C (from $CHCl_3$); $\nu_{max.}$($CHCl_3$) 3 300 (NH), 1 682 (amide I band), and 1 547 cm^{-1} (amide II band); δ_H (200 MHz; $CDCl_3$) 1.42 (3 H, t, *J* 7.2 Hz, C-Me), 3.09 (3 H, d, *J* 5.0 Hz, collapsed to singlet by adding D_2O, NH-*Me*), 4.40 (2 H, q, *J* 7.2 Hz, CH_2), 7.42 (1 H, dd, *J* 7.8 and 1.4 Hz, 5-H), 7.45 (1 H, ddd, *J* 7.8, 7.8, and 1.4 Hz, 7-H), 7.71 (1 H, ddd, *J* 7.8, 7.8, and 1.4 Hz, 6-H), 8.21 (1 H, dd, *J* 7.8 and 1.4 Hz, 8-H), and 9.68 (1 H, s, NH); δ_C($CDCl_3$) 162.4 (s), 154.8 (s), 144.8 (s), 133.0 (s and d), 132.7 (s and d), 124.5 (d), 113.6 (d), 38.0 (t), 26.6 (q), and 12.4 (q) (Found: *m/z* 231.1006. $C_{12}H_{13}N_3O_2$ requires *M*, 231.1008).

Synthesis of the Quinoxalinecarboxamide (**16a**).—A solution of *N*-phenyl-*o*-phenylenediamine (52.0 mg, 0.28 mmol) and diethyl oxomalonate (0.04 ml, 0.28 mmol) in dry xylene (5 ml) was refluxed for 43 h under an argon atmosphere.[26] The reaction mixture was concentrated to dryness and the residue was subjected to preparative t.l.c. [hexane–ether (3:7)] to give *ethyl* 4-*phenyl*-3-*oxo*-3,4-*dihydroquinoxaline*-2-*carboxylate* (**18a**) (68.3 mg, 82.4%); $\nu_{max.}$($CHCl_3$) 1 735 and 1 665 (CO) cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.40 (3 H, t, *J* 7.0 Hz, C-Me), 4.39 (2 H, q, *J* 7.0 Hz, CH_2), 6.55 (1 H, m, 5-H), 7.02—7.47 (7 H, m, Ar*H*), and 7.78 (1 H, m, 8-H); (Found: *m/z* 294.1007. $C_{17}H_{14}N_2O_3$ requires *M*, 294.1004). To a solution of the carboxylate (**18a**) (59.5 mg, 0.20 mmol) in ethanol (2 ml) was added methylamine (40% aqueous solution; 2 ml) and the mixture was stirred at room temperature for 5 min under argon atmosphere. The mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$), and evaporated to dryness to afford a crystalline mass. Recrystallisation of this from ether–$CHCl_3$ afforded the quinoxalinecarboxamide (**16a**) as yellow prisms (54 mg, 95.6%), m.p. 251—252 °C. The i.r. and ^1H n.m.r. were identical with those of (**16a**) obtained by hydrolysis of the spirohydantoin (**6a**).

Synthesis of the Quinoxalinecarboxamide (**16e**).—A mixture of ethyl 3-oxoquinoxaline-2-carboxylate[27] (125.8 mg, 0.58 mmol) and sodium hydride (50% in mineral oil; 36.9 mg, 0.77 mmol) in dry DMF (15 ml) was stirred at room temperature under an argon atmosphere. The mixture was stirred for 40 min after which ethyl bromide (0.06 ml, 0.80 mmol) was added and the whole refluxed for 6 h. The mixture was poured into aqueous $NaHCO_3$ and extracted with ethyl acetate. The extract was washed with brine, dried (K_2CO_3), and evaporated. The residue was chromatographed and elution with ether–hexane (1:9) gave ethyl 3-ethoxyquinoxaline-2-carboxylate (**19**)[27] (14.9 mg, 10.5%), $\nu_{max.}$($CHCl_3$) 1 735 (CO), 1 132, and 1 090 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.46 (3 H, t, *J* 7.1 Hz, C-Me), 1.49 (3 H, t, *J* 7.1 Hz, C-Me), 4.53 (2 H, q, *J* 7.1 Hz, CH_2), 4.61 (2 H, q, *J* 7.1 Hz, CH_2), 7.58 (1 H, ddd, *J* 8.3, 8.1, and 1.5 Hz, 6-H), 7.72 (1 H, ddd, *J* 8.3, 8.3, and 1.5 Hz, 7-H), 7.84 (1 H, dd, *J* 8.1 and 1.5 Hz, 5-H), and 8.08 (1 H, dd, *J* 8.3 and 1.5 Hz, 8-H); *m/z* (M^+). The mixture eluted with ether–benzene (1:1) was separated by preparative t.l.c. [methanol–$CHCl_3$ (6:94)]. From the less polar zone, *ethyl* 4-*ethyl*-3-*oxo*-3,4-*dihydroquinoxaline*-2-*carboxylate* (**18e**) was obtained (28.2 mg, 19.9%); $\nu_{max.}$($CHCl_3$) 1 735 and 1 660 cm^{-1} (CO); δ_H (60 MHz; $CDCl_3$) 1.37 (3 H, t, *J* 7.4 Hz, C-Me), 1.41 (3 H, t, *J* 7.4 Hz, C-Me), 4.25 (2 H, q, *J* 7.4 Hz, CH_2), 4.41 (2 H, q, *J* 7.4 Hz, CH_2), and 7.06—7.93 (4 H, m, Ar*H*). The more polar zone afforded 1-ethylquinoxalin-2-one as colourless prisms (8.9 mg, 8.9%), m.p. 61—62 °C (from $CHCl_3$) (lit.,[28] 64—65 °C); $\nu_{max.}$($CHCl_3$) 1 660 cm^{-1} (CO); δ_H (200 MzH; $CDCl_3$) 1.39 (3 H, t, *J* 7.2 Hz, C-Me), 4.32 (2 H, q, *J* 7.2 Hz, CH_2), 7.36 (1 H, ddd, *J* 7.5, 7.5, and 1.2 Hz, 6-H), 7.38 (1 H, d, *J* 7.5 Hz, 8-H), 7.60 (1 H, ddd, *J* 7.5, 7.5, and 1.5 Hz, 7-H), 7.90 (1 H, dd, *J* 7.5 and 1.5 Hz, 5-H), and 8.31 (1 H, s, 3-H); (Found: *m/z* 174.0795. $C_{10}H_{10}N_2O$ requires *M*, 174.1793). To a solution of the carboxylate (**18e**) (23.3 mg, 0.094 mmol) in ethanol (3 ml) was added methylamine (40% aqueous solution; 3 ml) and the mixture was stirred at room temperature for 10 min under argon atmosphere. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by preparative t.l.c. [methanol–$CHCl_3$ (6:94)] to give the quinoxalinecarboxamide (**16e**) as yellow needles (18.1 mg, 82.7%), m.p. 155—158 °C (from $CHCl_3$). The i.r. and ^1H n.m.r. were identical with those of (**16e**) obtained by hydrolysis of spirohydantoin (**6e**).

Crystal Structure Determinations.—(*a*) *Spirohydantoin* (**6a**)·$(CD_3)_2SO$. $C_{17}H_{14}N_4O_3 \cdot C_2D_6OS$, *M* = 406.5, monoclinic, space group $P2_1a$, *a* = 16.844(8), *b* = 10.806(3), *c* = 10.720(4) Å, β = 96.69(3)°, *U* = 1 937.9 Å^3, *Z* = 4, D_c = 1.372 g cm^{-3}, $R(R_w)$ = 0.088 (0.090) for 2 509 unique reflections [$F_o > 3\sigma(F_o)$].

(*b*) 1-*Methyl*-7,8-*diphenyl*-1,2,3,6-*tetrahydropurine*-2,6-*dione* (**B**). $C_{18}H_{14}N_4O_2$, *M* = 318.3, triclinic, space group *P*1, *a* = 11.147(1), *b* = 10.600(1), *c* = 7.237(1) Å, α = 110.04(1)°, β = 84.38(1)°, γ = 109.04(1)°, *U* = 759.3 Å^3, *Z* = 2, D_c = 1.392 g cm^{-3}, $R(R_w)$ = 0.051 (0.082) for 2 318 unique reflections [$F_o > 3\sigma(F_o)$]. In each case, a crystal with dimensions of 0.15 × 0.20 × 0.30 mm was used for data collection. The intensity data were collected on a Rigaku AFC-5RU diffractometer for 0 < θ < 60° using monochromated Cu-K_α radiation (λ = 1.541 78 Å), and the ω—2θ scan method at an ω scan speed of 16° min^{-1}. Three standard reflections were measured every 56 reflections to monitor intensity fluctuations. Absorption corrections were not applied. The structure was solved by the direct method using MULTAN program[29] and was refined by the full-matrix least-squares method, minimizing the function $\Sigma_\omega(|F_o| - |F_c|)^2$ with $\omega = 1/\sigma^2$. The hydrogen atoms were located from the D-map and refined with the isotropic thermal parameters. All computations were performed on a FACOM M 382 computer in the Data Processing Centre of Kyoto University, using the KPPXRAY programs.[30] Tables of the hydrogen atomic co-ordinates and the anisotropic thermal parameters are available on request from the Cambridge Cyrstallographic Data Centre.* Structure factors are available from the Editorial office.

* See Instructions for Authors (1987) para. 5.6.3, in *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

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