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PHOTOCHEMISTRY—XIII[1]

THE PHOTOISOMERIZATION OF PYRIDAZINE 1,2-DIOXIDES: FORMATION OF 3a,6a-DIHYDROISOXAZOLO[5,4-d]ISOXAZOLE

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Abstract—Products, generated from a photolysis of 1,2-dioxides (**1**) of unsubstituted (**a**), 3-Me-(**b**), 4-Me-(**c**), 3,6-diMe (**d**), 3-Ph-(**e**), 3-Me-6-Ph-(**f**) and 3,6-diPh-(**g**) pyridazines, have been investigated.

Dioxides (**1a-g**) afforded 3a,6a-dihydroisoxazolo[5,4-d]isoxazoles (**2a-g**). Dioxides (**1e** and **1g**) afforded 3-phenylisoxazole(**7**) besides **2**. The structure of **2a** was examined by X-ray crystallography.

The compound **2d** was also obtained by oxidation of the hexa-3-ene-2,5-dione dioxime. A mechanism generating those products has been speculated.

In the previous communications,[2,3] we have described that UV-irradiation of pyridazine 1,2-dioxides (**1**) afforded photo-isomers.

The structure of the photo-isomers has been shown[3] to be a new ring system: 3a,6a - dihydroisoxazolo[5,4 - d]isoxazole (**2**; 2,6 - dioxa - 3,7 - diazabicyclo[3,3,0]octa - 3,7 - diene) which had been incorrectly assigned to 1,4,6,7 - dioxadiazocin (**3**) in our earlier paper.[2] In connection with this point, further details of the data and some additional data will be described in this paper.

The formation of the isomers **2** is in sharp contrast to the known information in the photo-reaction of pyridazine mono-oxides where the formation of cyclopropenyl ketones, furans[4] and acylpyrazoles,[5] and also the deoxygenation and an intermolecular oxygen transfer[6] take place (Scheme 1 and 2).

RESULTS AND DISCUSSION

On irradiation of **1a-g** in CH_2Cl_2 with high-pressure Hg lamp, the corresponding **2** were obtained in the yields shown in Table 1. Physical data of **2** are collected in Table 1.

The ^1H NMR spectrum of **2a** showed two sharp singlets at δ 7.38 (3- and 6-H) and 6.05 (3a- and 6a-H) with equal intensities and ^{13}C NMR of it showed two signals (δ from TMS) at 143.86 (3- and 6-C) and 88.38 (3a and 6a-C). The IR spectrum showed an absorption due to C=N stretching at 1590 cm^{-1}. Its mass spectrum showed a peak of *m/e* 112 (M^+) besides those of *m/e* 69 (M^+-CHNO) and 68 (M^+-CH_2NO). The compound (**2d**) showed ^1H NMR signals at δ 5.75 (2H,s,3a- and 6a-H) and 2.10 (6H, s, $CH_3 \times 2$) and ^{13}C NMR signals (δ from TMS) at 153.74 (3- and 6-C), 89.98 (3a- and 6a-C) and 10.56 (CH_3) and an IR absorption at 1589 cm^{-1}. Mass spectrum of **2d** showed a peak of *m/e* 144 (M^+) besides that of *m/e* 82 (base peak).

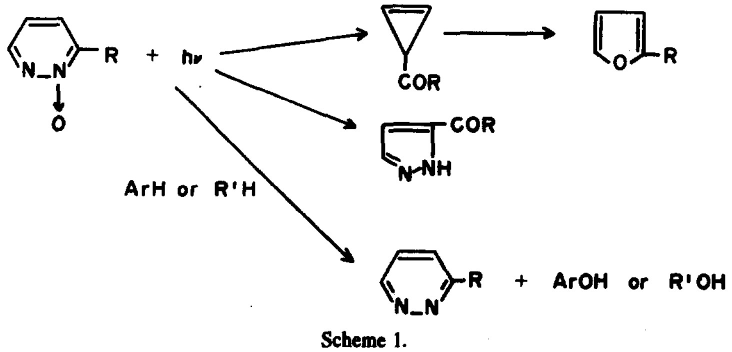
The latter was assignable to C_4H_4NO by high-resolution mass spectrometry (Found: 82.0285. Calc.: 82.0291) but not to $C_4H_6N_2$[2] (Scheme 3). UV spectra of **2a** and **2d** showed no absorption in the region > 220 nm (EtOH).

These data confirm that **2a** and **2d** have the structure of 3a,6a - dihydroisoxazolo[5,4-d]isoxazole (**2**).

Analogous data which satisfy the structure **2** have been obtained for **2b**, **2c**, **2e**, **2f** and **2g**.

Furthermore, **2a** was reduced with $NaBH_4$ in EtOH–THF to give **5a** (10%, yield) and then acetylated with Ac_2O to give **6a** (95%) (Scheme 4).

The ^1H NMR spectrum of **5a** showed signals at δ 7.22

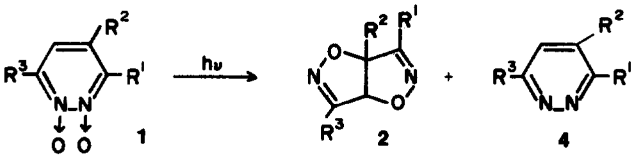


Scheme 1.

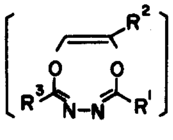
Table 1. Physical and spectral data of 2

	Yields(%)	m.p., b.p.	$M^+(m/e)$	cm^{-1}(C=N)	NMR (δ), J = Hz
2a	37	50–52	112	1590	6.05(2H, s, 3a- and 6a-H), 7.38(2H, s, 3- and 6-H).
2b	10	83–85/0.85*	126	1600	2.10(3H, s, 3-Me), 5.75(1H, d, 3a-H), 6.03(1H, d, 6a-H), 7.36(1H, s, 6-H), $J_{3a,6a}$ = 10.5.
2c	3	87–88/0.7*	126	1600	1.73(3H, s, 3a-Me), 5.59(1H, br.s, 6a-H), 7.22(1H, s, 3-H), 7.31(1H, br.s, 6-H).
2d	10	95–96	140	1615	2.10(6H, s, 3- and 6-Me), 5.75(2H, s, 3a- and 6a-H).
2e	23	107–108	188	1590	6.13(1H, d, 3a- or 6a-H), 6.25(1H, d, 3a- or 6a-H), $J_{3a,6a}$ = 8.0. 7.45–7.50(4H, m, 3-ph and 6-H), 7.75–7.85(2H, m, 3-ph).
2f	trace	102–103	202	1600	2.10(3H, s, 3-Me), 5.88(1H, d, 3a-H), 6.23(1H, d, 6a-H), 7.35–7.55(3H, m, 6-ph), 7.70–7.90(2H, m, 6-ph), $J_{3a,6a}$ = 9.8.
2g[11]	45	176–177	264	----	6.45(2H, s, 3a- and 6a-H), 7.30–7.65(6H, m, Ph), 7.70–7.95(4H, m, Ph)

*bath temperature.



1	2
a: $R^1 = R^2 = R^3 = H$	37%
b: $R^1 = Me$, $R^2 = R^3 = H$	10
c. $R^1 = R^3 = H$, $R^2 = Me$	3
d: $R^1 = R^3 = Me$, $R^2 = H$	10



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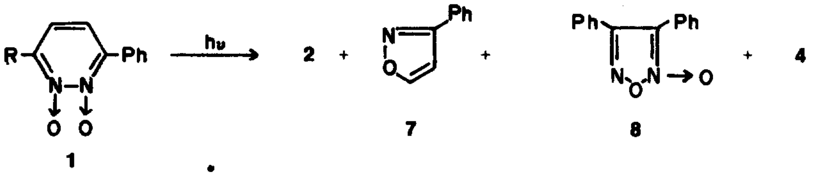
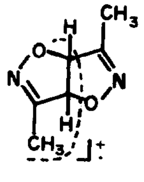


1	2	7	8
e: R = H	23%	trace	--
f: R = Me	trace	14%	--
g: R = Ph	45%	trace	trace

Scheme 2.



Scheme 3.

(1 H, br.s, 6-H), 5.67 (1 H, br.d, J = 6.4 Hz, 6a-H), 5.35 (1 H, dd, J = 6.4 and 3.6 Hz, 3a-H), 5.15 (1 H, br.s, NH), 3.56 (1 H, br.d, J = 13.6 Hz, 3-H') and 3.18 (1 H, dd, J = 13.6 and 3.6 Hz, 3-H) the latter two being coupled with each other. IR spectrum of **6a** (m.p. 104–105°) showed an absorption at 1670 cm^{-1} (C=O, KBr) and ^1H NMR spectrum exhibited the signals at δ 7.35 (1 H, br.s, 6-H), 5.74 (1 H, br.d, J = 7.0 Hz, 6a-H), 5.38 (1 H, dd, J = 7.0 and 4.0 Hz, 3a-H), 4.68[†] (1 H, br.d, J = 13.0 Hz, 3-H'), 3.38 (1 H, dd, J = 13.0 and 4.0 Hz, 3-H) and 2.10 (3 H, s, $COCH_3$).

These observations show that **5a** and **6a** have geminal protons (3-H and 3-H', J = 13.6 Hz in **5a** and 13.0 Hz in

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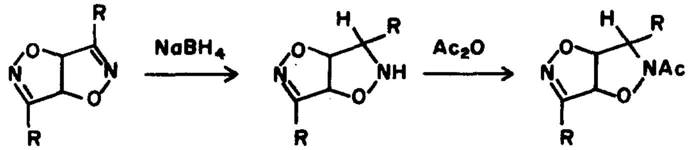
[†] By acetylation of NH, same down-field shift of the proton on a carbon adjacent to a nitrogen atom has been observed in a similar ring system.[7]



2a: R = H
2d: R = Me

5

6

Scheme 4.

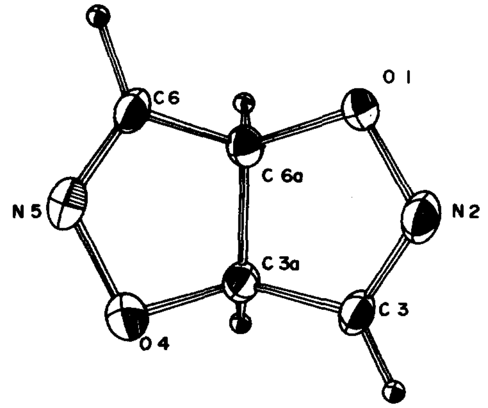


Fig. 1. Molecular structure of **2a**.

6a), having ABXY spin systems (*i.e.* -CH-CH-CHH'- moieties).

The compound **2d** also afforded **5d** (8%) and **6d** (90% from **5d**) and these products showed satisfactory spectral data (Experimental). These data are consistent with the expected products derived from **2** and inconsistent with those derived from **3**.

Moreover, to obtain direct information on the structure of **2**, X-ray analysis was carried out on a single crystal of **2a** (a needle from *i*-Pr_2O). Crystal data are as follows; space group $P2_1/n$, a = 8.24, b = 11.18, c = 5.35 Å and β = 102.76°, Z = 4.

The structure was solved by the direct method,[8] and refined by block diagonal least squares method to an R-factor of 0.06 on 565 independent reflections with $I > 3\sigma(I)$, within the limit $\theta < 60°$, obtained by Phillips automatic four circle difractometer (CuK_α-radiation). The final atomic coordinates are listed in Table 3 (Experimental).† Bond distances and bond angles thus obtained are shown in Table 2 and the crystallographic structure is shown in Fig. 1.

Irradiation of 3-phenylpyridazine 1,2-dioxides (**1e-g**) led to somewhat different results compared with the cases of **1a-d**.

Thus, **1e**, **1f** and **1g** gave 3-phenylisoxazole (**7**) besides **2** and **4** (Scheme 2). Dioxide **1g** gave diphenylfuroxan (**8**) in addition to **2**, **4** and **7**.

Additionally, no detectable amount of cyclopropenyl ketone or furan was generated in the attempted photoreaction, while the formation of parent pyridazines **4** was observed in 3–20% yield.

Further, the irradiation of **1a-g** in benzene or in methanol also afforded products described above, respectively, and no remarkable solvent effect was observed, while the irradiation of **1a-d** in benzene gave *ca.* 20%‡ of phenol.

The simplest mechanism of the production of **2** would involve a cleavage of the N_1-N_2 bond in **1** in the initial stages of the irradiation. The formation of these products can be rationalized by assuming the key intermediate, bis-iminoxyl radical **9**. The compounds **2** would form *via* re-cyclization of the radicals **10** generated from **9**. The products **7** and **8** could be provided by the elimination of the nitrile oxide (**11**) from **2** because irradiation of **2g** under the same conditions gave **7** (30%) and **8** (8%).

Table 2. Bond distances (Å) and angles (deg.) for structure of **2a**

O(1)-C(6a)	1.457(5)	N(2)-O(1)-C(6a)	109.0(3)
O(1)-N(2)	1.405(4)	O(1)-N(2)-C(3)	109.9(3)
N(2)-C(3)	1.254(4)	N(2)-C(3)-C(3a)	114.2(4)
C(3)-C(3a)	1.498(5)	C(3)-C(3a)-C(6a)	101.4(3)
C(3a)-C(6a)	1.493(6)	C(3)-C(3a)-O(4)	110.8(3)
C(3a)-O(4)	1.452(5)	O(4)-C(3a)-C(6a)	105.9(3)
O(4)-N(5)	1.418(5)	C(3a)-O(4)-N(5)	108.3(3)
N(5)-C(6)	1.257(6)	O(4)-N(5)-C(6)	109.2(4)
C(6)-C(6a)	1.480(5)	N(5)-C(6)-C(6a)	115.1(4)
		O(1)-C(6a)-C(6)	111.1(3)
		O(1)-C(6a)-C(3a)	105.4(3)
		C(3a)-C(6a)-C(6)	101.3(3)

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†The final values for the thermal parameters and structure factors have been deposited to the Cambridge Crystallographic Data Center, Univ. Chem. Lab., Lensfield Road, Cambridge CB2 1EW, England.

‡This yield is lower than that of phenol obtained by an irradiation of pyridazine mono-oxide in benzene.[6]

Furoxan **8** can be reasonably formed by dimerization[9] of **11** although other furoxans have not been isolated even in the cases of **1e** and **1f**.

A close rationalization in terms of the substituent effect in the preference for the course has not been made, and, cyclization of dinitroso compound **12**, which has not been isolated, could also be taken into consideration for the formation of **2**.[10]

To confirm the substantiality of the intermediate **9**, oxidation of dioxine **13** with phenyliodoso bistrifluoroacetate (**14**) has been reinvestigated. Spyroudis *et al.*[11] reported that oxidation of **13** with **14** afforded dioxide **1d**, although a clear mechanism has not been shown.

Formation of **9** could be expected[12,13] in the oxidation of **13**. Actually, it gave **2d** (5%) besides dinitro compound **15** (2.2%) and **1d** (15.2%). This observation may support the presence of **9** to give **2** not only in this oxidation, but also in above described photo-isomerization.

EXPERIMENTAL

All m.ps are uncorrected. IR spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra were recorded on a Hitachi RMS-4 and a Hitachi high resolution MS RMU-7L spectrometers. NMR spectra were run on a Hitachi R-20 (60 MHz, ^1H), R-22 (90 MHz, ^1H) and a JEOL-FX-100 (100 MHz, ^{13}C) spectrometers. UV spectra were run on a Hitachi EPS-3T instrument.

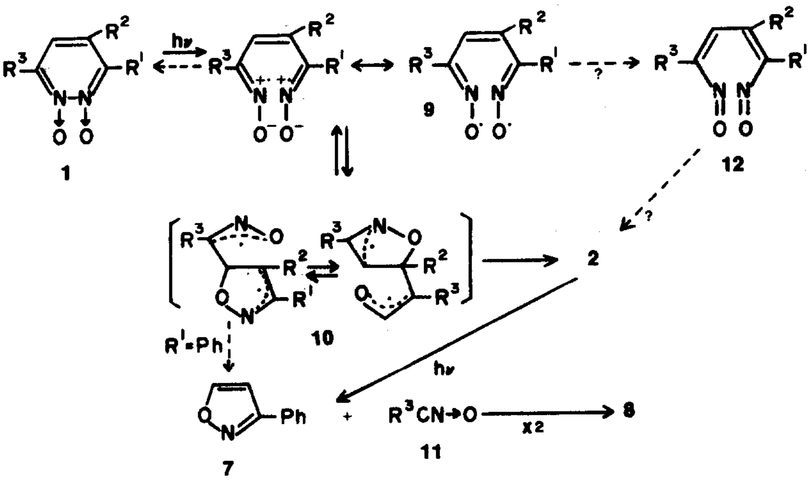
Preparation of **1**. Compounds **1a–e** were prepared according to the method reported.[14] **1f** and **1g** were prepared by the oxidation of the corresponding 2-unsaturated 1,4-diketone dioximes with lead tetraacetate.[17]

Compound **1f**: needles from AcOEt, m.p. 181–182°, mass spectrum (*m/e*); 213 (M^+), (*Found*: C, 65.62; H, 5.10; N, 13.88. *Calc.* for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86%). NMR (δ): 7.70–7.95 (2H, m, Ph), 7.40–7.60 (3H, m, Ph), 7.10 (2H, br.s, 4- and 5-H), 2.55 (3H, s, Me).

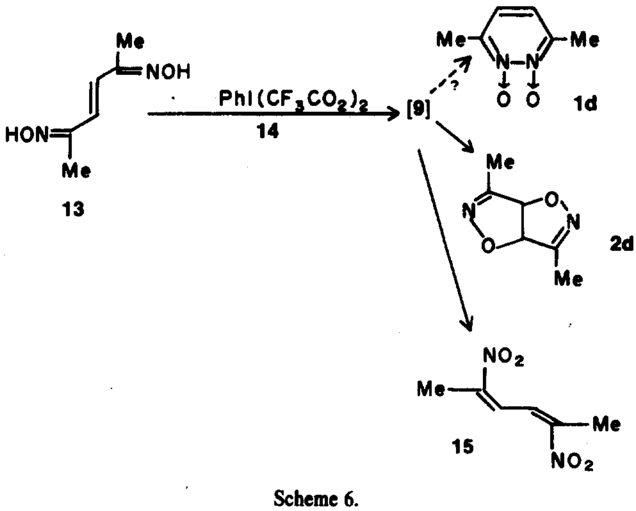
Compound **1g**; flakes from MeOH, m.p. 258° (dec),[18] mass spectrum (*m/e*) 264 (M^+), (*Found*: C, 72.97; H, 4.56; N, 10.54. *Calc.* for $C_{16}H_{12}N_2O$: C, 72.71; H, 4.58; N, 10.60%). NMR (δ): 7.85–8.00 (4H, m), 7.40–7.66 (8H, m), IR (KBr): 825, 1350, 1398 and 1460 cm^{-1}.

Photolysis of **1**. A solon of an **1** (0.2 g) in CH_2Cl_2 (200 ml) was irradiated under N_2 using a 200 W high pressure mercury lamp (Nikko Sekiei Co. Japan) for 4–6 hr until all the starting material had been consumed (tlc and vpc). A considerable amount of insoluble black residue was deposited in each run. The solvent was removed *in vacuo*. The mixture was chromatographed over silica gel column chromatography using benzene as an eluent to give **2** and **7** (from **1e–g**). From CH_2Cl_2 elution, **4** and **8** (from **1g**) were obtained.

Physical data and spectral data of **2a–g** are shown in Table 1. Compound **2a**: (*Found*: C, 42.62; H, 3.55; N, 24.98. *Calc.* for $C_4H_4N_2O_2$: C, 42.86; H, 3.57; N, 25.00%). Compound **2b**: high mass spectrum (*m/e*); M^+ *Calc.* for $C_5H_6N_2O_2$: 126.043. *Found*:



Scheme 5.



Scheme 6.

Table 3. Positional and thermal parameters for **2a** and their standard deviations

Atom	X	Y	Z
C(3)	0.0581(5)	0.1598(3)	1.0651(8)
C(3a)	-0.0041(5)	0.2861(3)	1.0342(7)
C(6a)	0.0301(5)	0.3182(3)	0.7802(7)
C(6)	0.1606(5)	0.4104(3)	0.8541(8)
O(1)	0.0971(4)	0.2099(2)	0.6897(5)
O(4)	0.1002(4)	0.3644(3)	1.2192(5)
N(2)	0.1151(4)	0.1220(3)	0.8814(7)
N(5)	0.2009(5)	0.4330(3)	1.0898(8)
H'C3	0.056(4)	0.105(4)	1.195(9)
H'C3a	-0.121(6)	0.293(4)	1.053(8)
H'C6a	-0.060(5)	0.348(4)	0.632(8)
H'C6	0.211(5)	0.459(4)	0.726(8)

Atom	$\beta_{1,1}$	$\beta_{2,2}$	$\beta_{3,3}$	$\beta_{1,2}$	$\beta_{1,3}$	$\beta_{2,3}$
C(3)	0.0178(8)	0.0050(3)	0.0048(19)	-0.0002(4)	0.0114(9)	0.0017(6)
C(3a)	0.0152(6)	0.0057(3)	0.0384(17)	-0.0002(4)	0.0010(8)	-0.0005(6)
C(6a)	0.0152(7)	0.0059(3)	0.0381(16)	0.0008(4)	0.0086(8)	0.0004(6)
C(6)	0.0180(8)	0.0049(3)	0.0526(21)	-0.0008(4)	0.0116(10)	0.0019(7)
O(1)	0.0248(6)	0.0066(2)	0.0466(13)	-0.0003(3)	0.0174(7)	-0.0016(5)
O(4)	0.0314(8)	0.0068(3)	0.0384(13)	-0.0009(4)	0.0091(8)	-0.0024(5)
N(2)	0.0195(7)	0.0051(3)	0.0565(17)	0.0002(4)	0.0137(8)	-0.0000(6)
N(5)	0.0214(8)	0.0056(3)	0.0646(20)	-0.0013(4)	0.0050(10)	0.0003(6)
H'C3	4.6955					
H'C3a	3.8259					
H'C6a	2.7857					
H'C6	3.8104					

126.045. Compound **2c**: high mass spectrum (*m/e*): M$^+$ *Calc.* for $C_5H_6N_2O_2$: 126.043. *Found*: 126.046. Compound **2d**: (*Found*: C, 51.39; H, 5.65; N, 19.98. *Calc.* for $C_6H_8N_2O_2$: C, 51.43; H, 5.71; N, 20.00%). Compound **2e**: (*Found*: C, 64.24; H, 4.49; N, 14.93. *Calc.* for $C_{10}H_8N_2O_2$: C, 63.83; H, 4.26; N, 14.89%). Compound **2f**: (*Found*: C, 65.36; H, 4.96: N, 13.86. *Calc.* for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86%). The compounds **7**[15] and **8**[9] were identical with the authentic samples.

Oxidation of **13** *with* **14**. Compound **13** was treated as described[11] and **1d** was filtered off. The mother liquor was evaporated and the residue was chromatographed over silica gel. Besides 15.2% of **1d** (m.p. 216°[11]), 2.2% of **15** (m.p. 160°, the physical data were identical with those described[16]) and 5% of **2d** (m.p. 95–96°) were obtained.

X-ray analysis of **2a**. Crystallography was carried out as described in the text. The final atomic coordinates are listed in Table 3.

Reduction of **2a** *and* **2d** *with* $NaBH_4$. To a solon of **2a** (100 mg) in EtOH–THF (1:5), $NaBH_4$ (30 mg) was added in small portions during 5–10 min, with cooling under stirring. After 4 hr, the ppt was removed by filtration. The solvent was evaporated and the residue was chromatographed over silica gel using CH_2Cl_2 as an eluent to give **5a**. Compound **2d** was treated as above to give **5d**. In both cases of **2a** and **2b**, the starting materials were recovered in about 20% yields.

Compounds **5a** was an unstable oil (yield 10%), NMR (δ): 3.18 (1 H, dd, *J* = 13.6 and 3.6 Hz, 3-H), 3.56 (1 H, br.d, *J* = 13.6 Hz, 3-H'), 5.15 (1H, br.s, NH), 5.35 (1H, dd, *J* = 6.4 and 3.6 Hz, 3a-H), 5.67 (1H, br.d, *J* = 6.4 Hz), 6a-H), and 7.22 (1H, br.s, 6-H).

Compound **5d** was an oil (yield *ca.* 8%), NMR (δ): 1.30 (3H, d, *J* = 7.0 Hz, 3-Me), 2.08 (3H, s, 6-Me), 3.40 (1H, m, 3-H), 5.07 (1H, dd, *J* = 7.0 and 4.0 Hz, 3a-H) and 5.49 (1H, d, *J* = 7.0 Hz, 6a-H), 4.55 (1H, br., NH). All attempts to detect the hexahydroisoxazoloisoxazoles in the reaction mixture failed.

Acetylation of **5a** *and* **5d**. A mixture of **5a** (20 mg) and Ac_2O (2 ml) was stirred for 1 hr at room temp., Ac_2O was evaporated *in vacuo* and the residue was chromatographed over silica gel to give **6a**. **5d** was treated as above to give **6d**.

Compound **6a**: m.p. 104–105° (from benzene), yield 95%, IR(KBr): 1670 cm^{-1} (C=O). NMR (δ): 2.10 (3H, s, $COCH_3$), 3.38 (1 H, dd, *J* = 13.0 and 4.0 Hz, 3-H), 4.68 (1 H, br.d, *J* = 13.0 Hz, 3-H'), 5.38 (1 H, dd, *J* = 7.0 and 4.0 Hz, 3a-H), 5.74 (1H, br.d, *J* = 7.0 Hz, 6a-H) and 7.35 (1H, br.s, 6-H). Mass spectrum (*m/e*): 156 (M$^+$). (*Found*: C, 46.27; H, 5.27; N, 17.85. *Calc.* for $C_6H_8N_2O_3$: C, 46.15; H, 5.13; N, 17.95%). Compound **6d**: a viscous oil, yield 90%. NMR (δ): 1.42 (3H, d, *J* = 7.0 Hz, 3-Me), 2.10 (3H, s, N-Ac or 6-Me), 2.12 (3H, s, N-Ac or 6-Me), 4.30 (1H, m, 3-H), 5.21 (1H, dd, *J* = 7.0 and 6.0 Hz, 3a-H) and 5.48 (1H, d, *J* = 7.0 Hz, 6a-H). High mass spectrum (*m/e*): M$^+$ *Calc.* for $C_8H_{12}N_2O_3$: 184.085. *Found*: 184.082.

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[18] The structure which had been assigned to **1g**[11] was not the compound.