STEREOSELECTIVITY OF CYCLOADDITIONS OF ARYLNITRILE OXIDES TO 5-ALKOXY-2(5*H*)-FURANONE*

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Dedicated to Prof. Jaroslav Kováč on the occasion of his 60th birthday.

1,3-Dipolar cycloaddition of arylnitrile oxides to 5-alkoxy-2(5*H*)-furanones (*II*) and 5-hydroxy-2(5*H*)-furanone leads regiospecifically to 4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazole derivatives *IIIa*—*IIIj*. The alkoxy derivatives give exclusively products of *exo*-configuration (*III*), whereas the hydroxy compound affords a 52 : 48 mixture of both diastereoisomers *IIIj* and *IVj*. Reaction of *III* with ammonia furnished diastereoisomeric tetrahydropyrrolo[3,4-*d*]isoxazoles *V* and *VI*, reaction with hydrazines led to hexahydroisoxazolo[4,5-*d*]pyridazin-7-one derivatives *VII*.

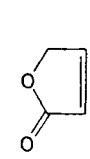
As found by Caramella and coworkers[1], cycloadditions of benzenenitrile oxide to *cis*-2,5-dimethoxy-2,5-dihydrofuran proceed stereoselectively *anti*- to the alkoxy substituent[1], reflecting the energetically favoured diaxial arrangement of the methoxy groups (anomeric effect). Moreover, *syn*-orientation of the oxygen-containing substituent relative to the oxygen atom of nitrile oxide leads to greater repulsion in the transition state[1]. The general interest in new stereoselectivite reactions and their utilization in organic synthesis prompted us to investigate the stereoselectivity of cycloadditions of nitrile oxides to 5-alkoxy-2(5*H*)-furanones (*II*).

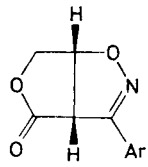
The interest in 5-substituted 2(5*H*)-furanones has increased since the finding that mucochloric and mucobromic acids exhibit marked bactericidal properties[2]. Also 5-hydroxy-2(5*H*)-furanone (*IIa*) is an effective bacteriostatic[3] and herbicide[4] and 5-ethoxy-2(5*H*)-furanone (*IIb*) (easily accessible by photooxidation of 2-furancarbaldehyde in ethanol) is the starting compound for syntheses of many biologically active compounds[5-8]. In spite of this, 1,3-dipolar cycloadditions of these compounds are practically unknown. The only addition described[9] is the reaction of phenyl azide with *IIb*.

Recently, we have found[10] that 1,3-dipolar cycloadditions of nitrile oxides to 2(5*H*)-furanone are regioselective affording head-to-tail cycloadducts *I*.

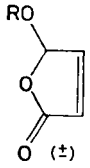
* Part XVII in the series 1,3-Dipolar Cycloadditions on Heterocycles; Part XVI: Chem. Papers, in press.

The 1,3-dipolar cycloaddition of (X-substituted)benzenenitrile oxides (where X is H, 4-CH_3, 4-F, 4-Cl, 3-Cl or 4-NO_2), as well as 2-furannitrile oxide and 9-anthracenenitrile oxide, to the furanone *IIb* afforded exclusively 3-aryl-4-oxo-6-ethoxy-3a, 4,6,6a-tetrahydrofuro[3,4-*d*]isoxazoles *IIIa–IIIj* of *exo*-configuration of the substituent in position 6. In principle, the reaction can lead to two regioisomeric pairs of *exo* and *endo* diastereoisomers (*III* and *IV*, respectively). The *endo*-isomers *IV*

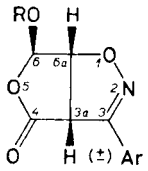




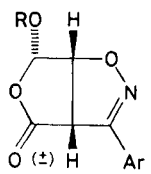
I



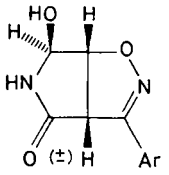
II



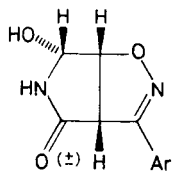
III a–III j



IV j



V a, b



VI a, b

In formulae *III – VI*: *a*, R = C_2H_5; Ar = C_6H_5
b, R = C_2H_5; Ar = 4-Cl—C_6H_4
c, R = C_2H_5; Ar = 4-F—C_6H_4
d, R = C_2H_5; Ar = 3-Cl—C_6H_4
e, R = C_2H_5; Ar = 4-O_2N—C_6H_4
f, R = C_2H_5; Ar = 4-CH_3—C_6H_4
g, R = C_2H_5; Ar = 9-anthryl
h, R = C_2H_5; Ar = 2-furyl
i, R = CH_3; Ar = C_6H_5
j, R = H; Ar = C_6H_5

were not detected even by careful ^1H and ^{13}C NMR analysis of crude reaction mixtures or mother liquors after filtration of *III*.

Structure of the compounds *III* was determined using ^1H and ^{13}C NMR spectra (Tables I–III) and compared with that predicted by a simple qualitative PMO analysis of 1,3-dipolar cycloadditions to *IIb*. The coupling constants $J_{6,6a}$ in the proton spectra should be about 0–3 Hz for the *exo*-adducts *III* and 5–8 Hz for the *endo*-compounds *IV* (ref.[1]). In the first approximation, the ethoxy group in position 5 of *IIb* should have no great effect on the values of atomic orbital coefficients in the parent 2(5*H*)-furanone[11,12]. Nitrile oxides containing an electron-accepting group bonded directly to the terminal carbon atom, such as methoxycarbonyl or cyano nitrile oxide, reacted neither with 2(5*H*)-furanone nor with *IIb*; this proves

TABLE I

3-Aryl-4-oxo-6-alkoxy-3a,4,6,6a-tetrahydrofuro[3,4-*d*]-isoxazoles *III*

Compound	Formula (M.w.)	M.p., °C Method, yield (%)	Calculated/found			λ_{max} (log ε) nm
			% C	% H	% N	
IIIa	$C_{13}H_{13}NO_4$ (247·2)	126–128 *A*, 45, *B*, 61[a]	63·15 63·26	5·30 5·22	5·67 5·71	263 (3·17)
IIIb	$C_{13}H_{12}ClNO_4$ (281·7)	120–122 *A*, 39, *B*, 57	55·42 55·36	4·26 4·31	4·97 5·05	271 (3·19)
IIIc	$C_{13}H_{12}FNO_4$ (265·2)	102–104 *A*, 34, *B*, 38	58·57 58·76	4·52 4·49	5·28 5·31	265 (3·05)
IIId	$C_{13}H_{12}ClNO_4$ (281·7)	80–82 *B*, 40	55·42 55·44	4·26 4·21	4·97 5·13	267 (3·07)
IIIe	$C_{13}H_{12}N_2O_6$ (292·2)	131–133 *A*, 34	53·43 53·38	4·14 4·22	9·59 9·61	302 (3·09)
IIIf	$C_{14}H_{15}NO_4$ (261·3)	98–100 *A*, 40, *B*, 38	64·36 64·61	5·79 5·52	5·36 5·47	268 (3·17)
IIIg	$C_{21}H_{17}NO_4$ (347·3)	185–187 *D*, 40	72·61 72·39	4·93 5·12	4·03 4·08	—
IIIh	$C_{11}H_{11}NO_5$ (237·2)	98–99 *B*, 40	55·69 55·92	4·67 4·58	5·91 5·93	281 (3·15)
IIIi	$C_{12}H_{11}NO_4$ (233·2)	109–111 *C*, 42	61·80 61·99	4·75 4·77	6·01 5·85	—
IIIj	$C_{11}H_9NO_4$ (219·2)	77–79 *C*, 45	60·27 60·33	4·14 4·08	6·39 6·49	—

[a] C, 41%.

that introduction of ethoxy group into the position 5 in 2(5*H*)-furanone does not change the dominating frontier orbital interaction HOMO (nitrile oxide)–LUMO (furanone)[10].

The structure of regioisomers *III*, as predicted from the PMO model, was confirmed by the δ values of signals in their NMR spectra (*e.g.* for *IIIa* 5·25 ppm (H-6a) and 4·71 ppm (H-3a) as well as 87·16 ppm (C_{6a}) and 54·05 ppm (C_{3a})) which are comparable with those of the adduct *Ia* (ref.[10]). The singlet at 5·65 ppm (H-6) in the ^{1}H NMR spectrum shows the configuration at the epimeric center in position 6. Signals of the *o*-aromatic protons (multiplet at 7·97–7·87 ppm) are separated from the remaining aromatic signals (7·47–7·36 ppm); this interesting fact may be ex-

TABLE II

^{1}H NMR spectral parameters of 3-aryl-4-oxo-6-alkoxy-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazoles *III*

Compound	Chemical shift, ppm (coupling constants, Hz)						
	H_{arom}	H_6	H_{6a}	H_{3a}	CH_2	CH_3	Others
IIIa	7·97–7·87 7·47–7·36	5·65 s	5·27 d (9·0)	4·71 d (9·0)	3·85 q	1·27 t	—
IIIb	7·62 d, d	5·62 s	5·27 d (9·0)	4·66 d (9·0)	3·82 q	1·25 t	—
IIIc	8·01–7·84 7·20–6·98	5·62 s	5·26 d (9·0)	4·67 d (9·0)	3·84 q	1·25 t	—
IIId	7·91–7·30	5·61 s	5·26 d (9·0)	4·62 d (9·0)	3·81 q	1·24 t	—
IIIe	8·35–8·05	5·69 s	5·36 d (9·0)	4·71 d (9·0)	3·86 q	1·29 t	—
IIIf	7·51d, d	5·62 s	5·24 d (9·0)	4·67 d (9·0)	3·82 q	1·26 t	2·36 (s, 3 H, CH_3)
IIIg	8·06–7·40	5·85 s	5·51 d (9·5)	4·86 d (9·5)	3·82 q	1·25 t	8·54 (s, 1 H, H-10′)
IIIh	—	5·59 s	5·22 d (9·5)	4·56 d (9·5)	3·66 q	1·24 t	7·53 (d, d, 1 H, H-5′) 7·06 (d, d, H, H-3′) 6·49 (m, 1 H, H-4′)
IIIi	7·97–7·85 7·53–7·38	5·53 s	5·26 d (9·0)	4·73 d (9·0)	—	3·56 s	—
IIIj	7·86–7·74 7·54–7·39	5·64 s	5·25 d (9·5)	4·70 d (9·5)	—	—	—

plained by a "bent" shape of the bicyclic system *III*. The ^{13}C NMR spectrum of *IIIa* displays signals typical of lactone (C=O 169·77 ppm) and isoxazoline (C=N 152·63 ppm) carbon atoms. The cycloadducts were obtained in yields ranging from

TABLE III

^{13}C NMR parameters of 3-aryl-4-oxo-6-alkoxy-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazoles *III*

Compound	Chemical shift, ppm							
	$C_{(3)}$	$C_{(3a)}$	$C_{(4)}$	$C_{(6)}$	$C_{(6a)}$	CH_2	CH_3	C_{arom}
IIIa	152·63	54·05	169·77	106·76	87·16	66·22	14·85	130·98 128·82 127·94 126·71
IIIb	151·84	54·05	169·64	106·94	87·51	66·27	14·81	137·22 129·23 125·49
IIIc	151·65	54·19	169·71	106·82	87·19	66·14	14·68	172·57 129·82 123·19 130·34
IIId	151·51	53·73	169·32	106·62	87·38	66·07	14·61	134·75 130·72 128·45 129·94 127·60 125·98
IIIe[a]	153·07	54·18	170·75	107·59	89·27	66·66	15·20	129·81 124·62
IIIf[b]	152·49	54·12	169·71	106·74	86·99	66·07	14·68	141·25 129·49 128·97 127·86
IIIh[c]	142·16	54·58	169·19	107·33	86·93	66·40	14·81	
IIIi	152·52	53·95	169·67	107·83	86·88	—	57·46	130·99 128·83 127·89 126·61

[a] Deuterated acetone; [b] 21·31 (q, CH_3); [c] furan ring: 145·54 (d, C(5′)), 144·37 (s, C(2′)), 115·78 (d, C(4′)), 112·01 (d, C(3′)).

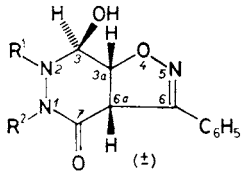
34% to 61%; as further product we isolated only nitrile oxide dimers[13]. 5-Methoxy-2(5*H*)-furanone reacted in analogous way giving *IIIi*. The NMR spectra of the anthryl and furyl derivatives *IIIg* and *IIIh*, respectively, exhibit slightly different chemical shifts (Tables II and III).

The observed stereospecificity of the 1,3-dipolar cycloaddition of nitrile to alkoxy derivatives *II* confirms the conclusions cited[1] in the introduction of this paper. To study the selectivity of the cycloaddition we chose another model system,5-hydroxy-2(5*H*)-furanone. With this compound, addition leading to *endo*-products could be favoured because of the possible hydrogen bond between the nitrile oxide oxygen atom and the hydroxyl hydrogen in *II*. In actual fact, the cycloaddition afforded a 52 : 48 miture of both diastereoisomers *IIIj* and *IVj* in 45% yield. We are able to isolate in the pure state only the derivative *IIIj* whose configuration was determined by the presence of H-6 singlet at 5·64 ppm, other values being in accord with the suggested structure (Tables II and III). The presence of the *endo*-diastereoisomer *IVj* (containing *IIIj*) was indicated by a multiplet of these protons at 6·16–5·90 ppm. containing an H-6 doublet with $J_{6-6a} = 4{\cdot}5$ Hz. No epimerization between *IIIj* and *IVj* was observed. The formation of the latter isomer can be explained by a hydrogen bond in the transition state, as mentioned above and as assumed already for other derivatives[14]. The 52 : 48 ratio indicates that in the addition to 5-hydroxy-2(5*H*)-furanone both effects leading to the *exo*- and *endo*-product are of about the same magnitude.

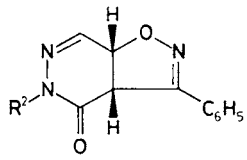
The 5-alkoxy-2(5*H*)-furanone grouping represents a significant precursor in the synthesis of 2(5*H*)-pyrrolines[15] and 3(2*H*)-pyridazinones[16], pharmacologically interesting compounds with long-lasting antihypertensive activity. We therefore tried to utilize the ethoxylactone structural unit of *III* in the preparation of condensed isoxazoline derivatives *V*–*VIII*. Reaction of *IIIa* with ammonia afforded a 1 : 1 mixture of both diastereoisomers *Va* and *VIa* of which we obtained in the pure state only the *exo*-adduct *Va*. Its structure, 3-phenyl-4-oxo-6-hydroxy-3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazole (*Va*), was confirmed by spectral data. The compound exists in the cyclic structure *Va* rather than in the formylamide structure as shown by chemical shift of the $C_{(6)}$ signal (89·73 ppm) in the ^{13}C NMR spectrum. The *exo*-configuration of the hydroxy group follows from the H-6 signal which appears as a singlet.

Reaction of *IIIb* with ammonia gave analogous results. The ratio of both diastereoisomers *Vb* and *VIb* was again 1 : 1 but in this case both isomers were isolated in the pure state. The ^1H NMR spectrum of *Vb* exhibits a singlet at 4·99 ppm (H-6) and doublets of the bridge protons H-6a (4·91 ppm) and H-3a (4·65 ppm). On the other hand, in the spectrum of *VIb* the H-6 and H-6a signals appear as a multiplet at 5·46–5·32 ppm and the H-3a signal is located at 4·70 ppm. The multiplicity of H-6 signals and their downfiled shift relative to those for *Vb* confirm the *cis*-relationship of the hydrogen atoms H-6 and H-6a in *VIb*.

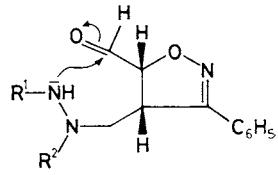
Very interesting results were obtained in the reaction of *IIIa* with hydrazines. In contrast with the published data[16], the reaction of *IIIa* with hydrazine in boiling aqueous acetic acid gave, instead of the expected 6-phenyl-1,3a,6a,7-tetrahydroisoxazolo[4,5-*d*]pyridazine-7-one (*VIII*), its precursor 3-hydroxy-6-phenyl-1,2,3,3a,6a,7-hexahydroisoxazolo[4,5-*d*]pyridazine-7-one (*VIIa*). Interestingly, of the two



VII a - VII c



VIII



IX

In formulae *VII*, *IX*: *a*, $R^1 = R^2 = H$; *b*, $R^1 = H$; $R^2 = CH_3$; *c*, $R^1 = C_6H_5$; $R^2 = H$

In formula *IX* amide carbonyl group is not shown.

possible diastereoisomers the reaction gave only the *exo*-isomer in which the H-3 hydrogen atom is *trans* to the H-3a and H-6a bridge hydrogen atoms (H-3 appears as a singlet in the ^{1}H MNR spectrum). The hydroxy derivative *VIIa* showed molecular peak $M^{+\cdot}$ of *m/z* 233 and an $M^{+\cdot} - OH$ fragment in the mass spectrum (instead of *m/z* 215 expected for *VIII*). The structure was confirmed by the presence of an H-3 singlet at 4·94 ppm in the ^{1}H NMR spectrum and a $C_{(3)}$ doublet in the ^{13}C NMR spectrum, as well as by the absence of a low-field —CH=N signal, expected for *VIII*. The reaction with phenylhydrazine and methylhydrazine proceeded in the same manner, giving again the analogous compounds *VIIc* and *VIIb*, respectively, as the sole products. The stereospecific formation of the *exo*-derivatives *VIIa*–*VIIc* can be explained by smaller repulsive interactions in the transition state on the way from intermediate *IX* to the product *VII* than in the transition state leading to the *endo*-stereoisomer. The stereospecificity of this reaction contrasts with the complete lack of selectivity in the above-mentioned formation of the five-membered ring derivatives *V* and *VI*. The described method, starting from the easily accessible 5-ethoxy-2(5*H*)-furanone, allows a simple high-yield (50–85%) synthesis of condensed isoxazolines, obtainable otherwise only with great difficulties.

EXPERIMENTAL

The melting points are uncorrected. ^{1}H NMR spectra were measured on a Tesla 487 C instrument, ^{13}C NMR spectra on a JEOL spectrometer, in deuteriochloroform (unless stated otherwise) using tetramethylsilane as internal standard. Ultraviolet spectra were recorded in methanol on a Perkin–Elmer 323 spectrometer in thermostated cells; values of ε are given in $m^2\ mol^{-1}$.

Mass spectra were taken on an MS 902 S instrument (direct inlet, ionization energy 70 eV, trap current 100 μA). The reaction course was monitored by TLC (Silufol plates, spots detected by UV light at 254 nm or by iodine vapour).

Chlorides of benzenehydroximic acids were prepared by chlorination of the corresponding benzaldoximes in chloroform according to ref.[17]. The preparation of 9-anthracenenitrile oxide was carried out as described[18], chloride of furanhydroximic acid was obtained by treatment of furaldoxime with nitrosyl chloride[19]. 5-Ethoxy- and 5-methoxy-2(5*H*)-furanone were synthesized by irradiation of 2-furancarbaldehyde with a 600 W medium pressure lamp in ethanol and methanol, respectively, in the presence of eosin and with introduction of a strong current of air, according to ref.[20]; 2-hydroxy-2(5*H*)-furanone was prepared by hydrolysis of the ethoxy derivative *IIb* (ref.[21]).

3-Aryl-4-oxo-6-alkoxy-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazoles *IIIa*—*IIIj*

Methods *A*—*D* were used. After the end of the cycloaddition, the reaction mixtures were processed as described, concentrated *in vacuo* and the products were triturated with the appropriate solvent or chromatographed on a column of silica gel and purified by crystallization from ethanol (*IIIi* from methanol).

Method A: Triethylamine (13 mmol) in dry ether (10 ml) was added at 0—5°C to a stirred and cooled solution of the corresponding hydroximic acid chloride (10 mmol) and the dipolarophile (10 mmol) in dry ether (30 ml) during 1 h. After stirring overnight at room temperature, the precipitated triethylamine hydrochloride was removed by filtration and the filtrate was worked up as described above.

Method B: The hydroximic acid chloride (10 mmol) in dry ether (50 ml) was added at room temperature during 4 h to a stirred solution of the dipolarophile (10 mmol) and triethylamine (13 mmol) in dry ether (10 ml). The further work-up procedure was the same as described under *A*.

Method C: The hydroximic acid chloride (30 mmol) was added portionwise during 10 min at about 0°C to a vigorously stirred mixture of 10% sodium hydroxide solution (20 ml) and ether (20 ml). The ethereal layer was separated, quickly dried (with stirring) over magnesium sulfate and added to a solution of the dipolarophile (30 mmol) in dry ether (10 ml). After stirring for 1 h at room temperature, the product was collected on filter or the mixture was concentrated and processed as described above.

Method D: The nitrile oxide (5 mmol) and dipolarophile (5 mmol) in dry benzene (25 ml) were heated to 80°C for 4 h. After cooling, the product was filtered or the mixture was concentrated and processed as described above.

Reaction of 3-Phenyl-4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazole (*IIIa*) with Ammonia

Methanolic ammonia (10%; 5 ml; 12 mmol) was added to a solution of isoxazoline *IIIa* (1 g; 4 mmol) in benzene (20 ml) and the mixture was set aside overnight at room temperature. The formed 1 : 1 mixture (^{1}H NMR spectrum) of diastereoisomeric 3-phenyl-4-oxo-6-hydroxy-3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazoles (*Va* and *VIa*) was filtered (quantitative yield) and chromatographed on a column of silica gel, eluant cyclohexane–ethyl acetate (1 : 3). Only the diastereoisomer *Va*, m.p. 168—170°C, was obtained in the pure form; yield 45%. For $C_{11}H_{10}N_2O_3$ (218·2) calculated: 60·54% C, 4·62% H, 12·84% N; found: 60·67% C, 4·33% H, 13·05% N. UV spectrum, λ_{max} (log ε): 265 (3·06). ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 8·04 to

7·84 (m, 2 H, aromatic H), 7·56—7·42 (m, 3 H, aromatic H), 5·20 (s, 1 H, H-6), 5·14 (d, J = = 9·0 Hz, 1 H, H-6a), 4·84 (d, 1 H, H-3a). ^{13}C NMR spectrum (hexadeuteriodimethyl sulfoxide): 170·76 (s, C=O), 154·66 (s, C=N), 130·25, 128·56, 128·04 (aromatic C), 89·73 (d, $C_{(6)}$), 82·07 (d, $C_{(6a)}$), 54·28 (d, $C_{(3a)}$).

Reaction of *IIIb* with Ammonia

Compound *IIIb* was treated with ammonia as described for *IIIa*, affording a 1 : 1 mixture of diastereoisomeric 3-(4-chlorophenyl)-4-oxo-6-hydroxy-3a,4,6,6a-tetrahydropyrrolo[3,4-*d*]isoxazoles *Vb* and *VIb* which were separated. Isomer *Vb*, m.p. 166—168°C. For $C_{11}H_9ClN_2O_3$ (252·6) calculated: 52·30% C, 3·56% H, 11·08% N; found: 52·45% C, 3·71% H, 11·00% N. ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·77 (d, 2 H, aromatic H), 7·41 (d, 2 H, aromatic H), 4·99 (s, 1 H, H-6), 4·91 (d, J = 9·0 Hz, 1 H, H-6a), 4·65 (d, 1 H, H-3a). Diastereoisomer *VIc*, m.p. 128—130°C. For $C_{11}H_9ClNO_3$ (252·6) calculated: 52·30% C, 3·56% H, 11·08% N; found: 52·16% C, 3·58% H, 10·99% N. ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 8·02 (d, 2 H, aromatic H), 7·62 (d, 2 H, aromatic H), 5·46—5·32 (m, 2 H, 6-H, 6a-H), 4·70 (m, 1 H, H-3a).

Reaction of *IIIa* with Hydrazines

A mixture of isoxazole *IIIa* (1·25 g; 5 mmol), acetic acid (4 ml), water (3 ml), and 80% aqueous hydrazine hydrate (0·7 g; 11 mmol) or methylhydrazine or phenylhydrazine was refluxed for 1·5 h. After cooling, the reaction mixture, obtained with hydrazine or phenylhydrazine, afforded a solid product which was filtered, dried *in vacuo* in a dessicator and crystallized from ethanol. With methylhydrazine, the reaction mixture was poured into a solution of sodium hydrogen carbonate, extracted with ether (3 × 20 ml), dried over sodium sulfate and concentrated *in vacuo*. The product *VIIb* was obtained by chromatography of the residue on a column of silica gel in cyclohexane–ethyl acetate (1 : 3).

3-*Hydroxy*-6-*phenyl*-1,2,3,3a,6a,7-*hexahydroisoxazolo*[4,5-*d*]*pyridazin*-7-*one* (VIIa), m.p. 173 to 174°C, prepared from hydrazine in 68% yield. For $C_{11}H_{11}N_3O_3$ (233·2) calculated: 56·65% C, 4·75% H, 18·02% N; found: 56·81% C, 4·72% H, 18·14% N. UV spectrum, λ_{max} (log ε): 260 (3·08). Mass spectrum, m/z: 233 ($M^{+\bullet}$), 215 ($M^{+\bullet} - 18$). ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·87—7·75 (m, 2 H, aromatic H), 7·36—7·20 (m, 3 H, aromatic H), 4·94 (s, 1 H, H-3), 4·85 (d, J = 9·5 Hz, 1 H, H-3a), 4·67 (d, 1 H, H-6a), 3·57 (s-br, 1 H, OH). ^{13}C NMR spectrum (hexadeuteriodimethyl sulfoxide): 165·74 (s, C=O), 154·44 (s, C=N), 130·21, 128·45, 127·80, 125·79 (aromatic C), 86·47 (d, $C_{(3a)}$), 84·98 (d, $C_{(3)}$), 53·15 (d, $C_{(6a)}$).

1-*Methyl*-3-*hydroxy*-6-*phenyl*-1,2,3,3a,6a,7-*hexahydroisoxazolo*[4,5-*d*]*pyridazine*-7-*one* (VIIb), prepared from methylhydrazine, m.p. 169—170°C, yield 50%. For $C_{12}H_{13}N_3O_3$ (247·2) calculated: 58·29% C, 5·30% H, 17·00% N; found: 58·21% C, 5·24% H, 16·88% N. Mass spectrum, m/z: 247 ($M^{+\bullet}$). ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·89—7·70 (m, 2 H, aromatic H), 7·37—7·21 (m, 3 H, aromatic H), 5·04 (m, 2 H, H-3a, H-6a), 4·78 (s, 1 H, H-3), 3·26 (s, 3 H, CH_3).

2,6-*Diphenyl*-3-*hydroxy*-1,2,3,3a,6a,7-*hexahydroisoxazolo*[4,5-*d*]*pyridazin*-7*one* (VIIc), prepared from phenylhydrazine, m.p. 193—195°C, yield 85%. For $C_{17}H_{15}N_3O_3$ (309·3) calculated: 66·01% C, 4·89% H, 13·59% N; found: 66·13% C, 5·02% H, 13·51% N. Mass spectrum, m/z 309, ($M^{+\bullet}$). ^{1}H NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·86—7·74 (m, 2 H, aromatic H), 7·39—7·25 (m, 3 H, aromatic H), 7·15—6·41 (m, 5 H, aromatic H), 5·02 (d, J = 9·0 Hz, 1 H, H-3a), 4·67 (d, 1 H, H-6a), 4·64 (s, 1 H, H-3).

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