# PHOTOINDUCED REARRANGEMENT OF HYDROXYMETHYLISOXAZOLINES, A ROUTE TO ENAMINOALDEHYDES*

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3-Aryl-4-R-carbamoyl-5-hydroxymethylisoxazolines (*IV*) were synthesized by allowing R-$NH_2$ amines with R = H, $CH_3$, $C_3H_7$, $C_6H_5C_2H_5$, and $NH_2$ to act on 3-(X-phenyl)-4-oxo-3*a*,4,6,6*a*-tetrahydrofuro[3,4-*d*]isoxazoles (*III*) with X = H, 4-$CH_3$, 4-$OCH_3$, 2-$OCH_3$, 4-Cl, 2-Cl, 4-F, 2-F, 4-Br, 4-$NO_2$, and 3-$NO_2$. Exposed to radiation, the substances *IV* give *Z*-2-hydroxymethylamino-2-aryl-1-formylacrylamides (*V*) in goodyields. The 4-Cl and 4-F substituted *Z*-derivatives *V* isomerize irreversibly to the *E*-derivatives *VI* if allowed to stand in solvent; the remaining derivatives *V* are stable. The quantum yields of the photoreaction are from 0·012 to 0·106 in dependence on the substituent X. In all cases where the compounds *IV* were used for the preparation of condensed heterocycles in conditions of acid-catalyzed reactions, lactones *III* were preferentially formed; the action of thionyl chloride on *IV* results in the formation of chloromethyl derivatives *VIII*, which do not undergo further cyclization.

Isoxazoline derivatives have proved to be useful intermediates, particularly for the synthesis of γ-amino alcohols[1], β-hydroxycarbonyl compounds[2,3], and their derivatives[4]. Attempts were made to make use of the photochemistry of isoxazolines, the rearrangements, however, are usually nonselective[5-9]. We have found[10-15] that a highly selective photoinduced rearrangement leading to cyclic enaminoaldehydes, such as *I* → *II*, takes place if an oxygen atom has been introduced into the β-position with respect to the isoxazoline oxygen. Our next aim was to achieve a further generalization of this synthesis route. In the present work we report on the synthesis of some novel noncyclic enaminoaldehydes, where the crucial step is the preparation of isoxazolines possessing a hydroxymethyl group in position 4.

All reaction steps described in this paper proceed under mild reaction conditions and no complicated working-up is necessary. The synthesis of the readily preparable

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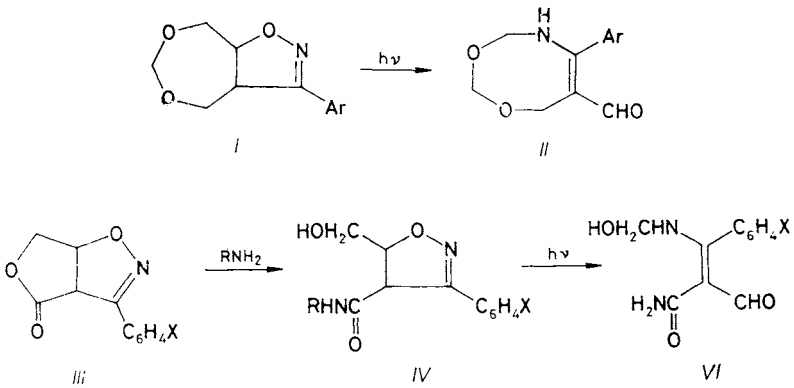
starting 3-(X-phenyl)-4-oxo-3*a*,4,6,6*a*-tetrahydrofuro[3,4-*d*]isoxazoles *IIIa*–*IIIj*, where X is H, 4-$OCH_3$, 4-$CH_3$, 4-Cl, 4-F, 4-Br, 2-$OCH_3$, 2-Cl, 4-$NO_2$, 3-$NO_2$, or 2-F, by 1,3-dipolar cycloaddition of benzenenitriloxides to 2-(5*H*)-furanone, has been described previously[16]. By the action of amino compounds R-$NH_2$ (R = H, $C_3H_7$, $CH_3$, or $C_6H_5C_2H_4$, Scheme 1) on *III*, we prepared 3-aryl-4-R-carbamoyl--5-hydroxymethylisoxazolines *IVa*–*IVt*. The reaction conducted at room temperature is complete in 12–24 h if a small excess of the amino compound is used. Benzene




*I* *II* *III* *IV* *VI*

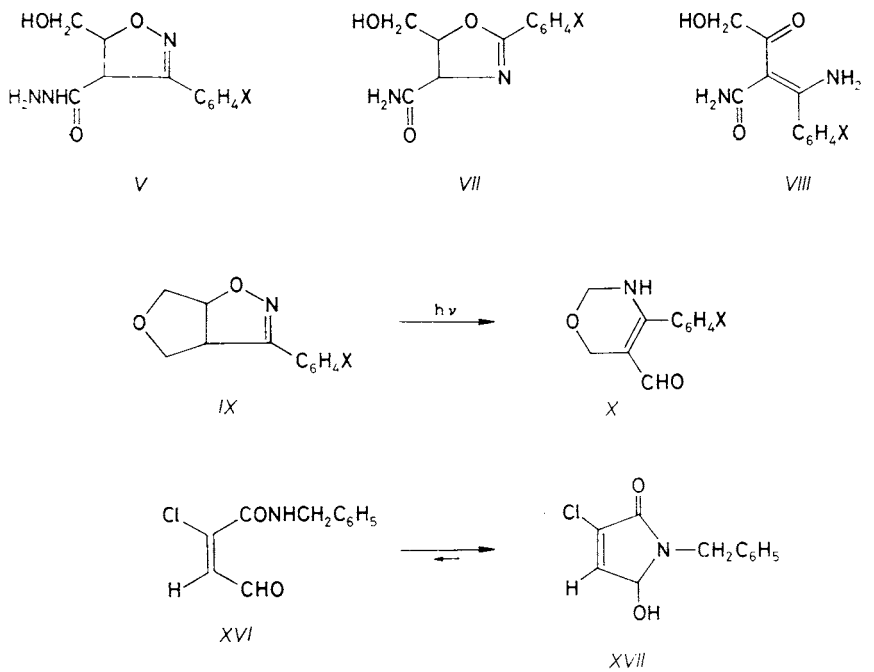
In formulae *III*, *V*, *VI*, *XXI*, *XXII*:
*a*, X = H; *b*, X = 4-$OCH_3$; *c*, X = 4-$CH_3$; *d*, X = 4-Cl; *e*, X = 4-F; *f*, X = 4-Br; *g* X = 2-$OCH_3$; *h*, X = 2-Cl; *i*, X = 4-$NO_2$; *j*, X = 2-F; *k* X = 3-$NO_2$.

*IV*: *a*, R = H; X = H; *b*, R = H; X = 4-$OCH_3$; *c*, R = H; X = 4-$CH_3$; *d*, R = H; X = 4-Cl; *e*, R = H; X = 4-F; *f*, R = H; X = 4-Br; *g*, R = H; X = 2-$OCH_3$; *h*, R = H; X = 2-Cl; *i*, R = $C_3H_7$; X = H; *j*, R = $C_3H_7$; X = 4-$OCH_3$; *k*, R = $C_3H_7$; X = 4-$CH_3$; *l*, R = $C_3H_7$; X = 4-Cl; *m*, R = $C_3H_7$; X = 4-F; *n*, R = $C_3H_7$; X = 4-Br; *o*, R = $C_3H_7$; X = 4-$NO_2$; *p*, R = $C_3H_7$; X = 3-$NO_2$; *r*, R = $C_6H_5CH_2CH_2$; X = H; *s*, R = $C_6H_5CH_2CH_2$; X = $OCH_3$; *t*, R = $CH_3$; X = 4-F.

SCHEME 1

appeared to be the most suitable solvent; the yields in it are 91–99%. The structure of the parent compound *IVa* is confirmed by the occurrence of the $^1H$ NMR multiplet

at 4·61 ppm (5-H) and doublet at 4·30 ppm (4-H) for the isoxazoline protons. The interaction constant, $J_{4,5}$ = 6·7 Hz, gives evidence of the *cis*-arrangement. The $^1$H NMR spectrum also exhibits a triplet of the hydroxy group (4·99 ppm), which shifts on heating and vanishes on adding heavy water, and a doublet-doublet of the methylene group at 3·50 ppm. The $^{13}$C NMR spectrum displays characteristic signals of the isoxazoline skeleton, *viz.* a singlet at 155·02 ppm (C=N) and doublets at 87·05 ppm ($C_{(5)}$) and 55·48 ppm ($C_{(4)}$). The structure of the side chains is borne out by the singlet of the amide group at 171·01 ppm (C=O) and a triplet of the methylene group at 62·11 ppm. The structure of the isoxazolines *IVb–IVt* was proved similarly. All the derivatives exhibit an absorption band in the UV spectrum at wavelengths characteristic of isoxazoline derivatives. Reacting *III* with hydrazine hydrate in benzene, we obtained substituted 3-aryl-4-aminocarbamoyl-5-hydroxymethylisoxazolines *V* in high yields; their structure was assigned as in the case of compounds *IV* (Scheme 2).



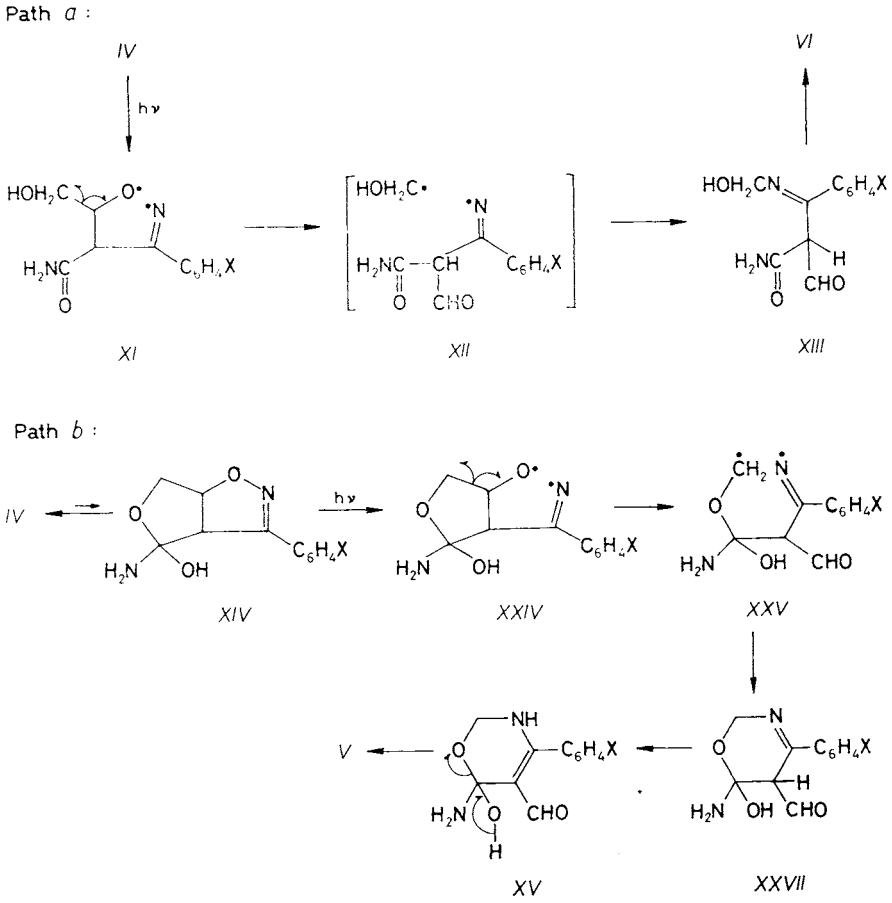

SCHEME 2

The UV spectra of the prepared isoxazolines *IV* indicate that radiation of wavelengths below 300 nm will be suitable for the photorearrangement. We employed monochromatic radiation $\lambda_{max}$ = 253·7 nm for the preparative photoreactions of compounds *IVa–IVe*. Photolysis of methanolic solutions of these compounds

gave rearrangement products *VIa–VIe*, respectively, in high yields (67–81%). Of the possible structures *VI*, *VII*, and *VIII* which could be deduced from literature data[5–15], the enaminoaldehyde structure of Z-2-hydroxymethylamino-2-aryl-1--formylacrylamide (*VIa–VIe*) was assigned based on the elucidation of the spectral data. For instance, the following evidence was gained for *VIa*: *a*) in the $^1$H NMR spectrum, occurrence of a singlet at 8·49 ppm due to the aldehyde proton; the signal does not change in position on heating or adding heavy water; *b*) in the $^{13}$C NMR spectrum, occurrence of singlet signals at 170·24 and 102·46 ppm due to the carbon atoms of the double bond of the enaminoaldehyde structure unit, and of a doublet signal at 188·16 ppm belonging to the aldehyde carbon atom; *c*) in the UV spectrum, bathochromic shift of the longest-wavelength band with respect to that at 284 ppm for the starting *IVa* compound, due to the presence of the conjugated chromophore grouping. The $^1$H NMR spectrum of *VIa* also contains two triplets at 8·83 ppm and 6·07 ppm (NH and OH), which shift on heating or adding heavy water. The multiplicity of the two signals bears out the presence of the $HOCH_2NH$ grouping; additional evidence is offered by the $^1$H NMR doublet-doublet of the methylene group at 4·27 ppm. The $^{13}$C NMR spectrum also indicates the presence of the amide and methylene group.

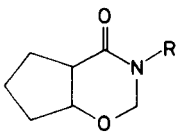
We suppose that derivatives of 2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*II*) and 2,3--dihydro-6*H*-1,3-oxazine (*X*), the mechanism of which has been dealt with in our previous papers[11–14], and enaminoaldehydes *VI* are formed basically by the same pathway (Scheme 3). Also in this case the formation of enaminoaldehydes *VI* solely must be due to the occurrence of the biradical which can be stabilized by the *p*-electrons of the oxygen atom. Two mechanism variants can be formulated as follows. In variant *a*, homolysis of the N—O bond in *IV* results in the formation of biradical *XI* whose fragmentation leads to the radical pair *XII* with the presumed stabilization (see above); subsequent recombination of *XII* gives amide *XIII*. A similar mechanism *via* a radical pair has been suggested by Padwa and Cohen for the rearrangement of 2-benzyloxyoxazoles[17]. The *XIII* formed undergoes 1,3-sigmatropic displacement to give enaminoaldehyde *VI* which is more favoured from the energy point of view. In variant *b*, only cyclic biradicals are considered. The first step includes the formation of *XIV*, the cyclic form of *IV*, whose subsequent photorearrangement is analogous to the *IX* → *X* conversion. In the last step, 4-aryl-5-formyl-6-amino-6-hydroxy-2,3--dihydro-6*H*-1,3-oxazine (*XV*) transforms into the more stable form of the enaminoaldehyde *VI* (Scheme 3). An equilibrium similar to that for *IV–XIV* has been suggested[18] for the system of aldehydoamines *XVI* and hydroxypyrrolidones *XVII*.

UV spectral monitoring during the photolysis of isoxazolines *IV* in low concentrations (50 μmol $l^{-1}$) using radiation 253·7 nm wavelength revealed the occurrence of isosbestic points at 243 and 284 nm (for *IVa*), which are indicative of an *A* → *B* type photochemical reaction; also, the ED (extinction difference) diagrams are linear. The reaction *IV* → *VI* proceeds with the same quantum yields in the presence and in

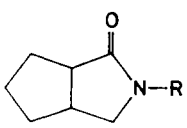



SCHEME 3

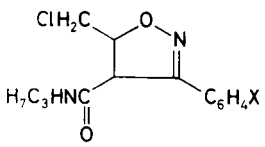
the absence of oxygen; therefore, we assume a singlet mechanism in agreement with published data[6-9]. The quantum yields $\Phi$ for the *IV* → *VI* photorearrangement, along with those for the *IX* → *X* rearrangement (which are lower than for *IV* → *VI*), are given in Table I. Previously[13,15,19] we observed that the $\Phi$ values decrease in the order of substituents bonded to the aromatic system for bicyclic derivatives $H > F > Cl > CH_3 > OCH_3$. In the *IV* → *VI* series, isoxazolines containing halogen atoms exhibit higher $\Phi$ values than the parent unsubstituted compound. It is also noteworthy that the $\Phi$ value increases on introducing a propyl into the carbamoyl group. For the propylcarbamoyl derivatives *IVi*–*IVm*, the photochemical rearrangement was monitored by UV spectroscopy only. The spectra indicate that the photorearrangement proceeds in the same manner as for derivatives *IVa*–*IVe*.



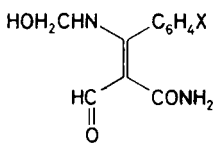
*XVIII*



*XIX*



*XXI*



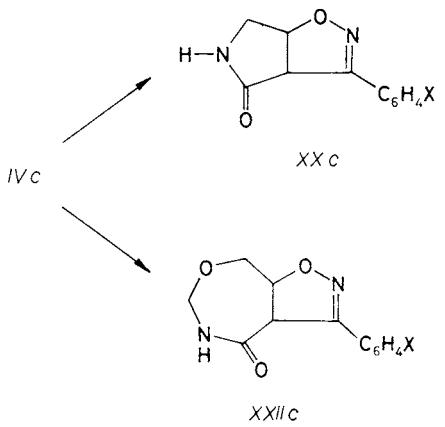
*XXIII d*, X = 4-Cl
*XXIII e*, X = 4-F

Furthermore, we paid attention to the use of the hydroxymethylcarbamoyl fragment in *IV* for the synthesis of heterocyclic compounds (Scheme 4), in view of the fact that the *cis*-2-hydroxy-1-carbamoyl grouping has been employed for the preparation of derivatives of 2,3,5,6-tetrahydro-1,3-oxazin-4-one *XVIII*, which is an antipyretic[20], and the *cis*-2-hydroxymethyl-1-carbamoyl fragment, for the synthesis[21] of the 2-pyrrolidone derivative *XIX*. We chose the conventional method, based on heating with thionyl chloride, for the preparation of the pyrrolidone derivatives *XX*. The chloro derivative intermediate then undergoes intramolecular cyclization to give the 2-pyrrolidone derivative. In our case, where amides *IV* were reacted with thionyl chloride in benzene at 90°C, only the corresponding 3-aryl-4-propylcarbamoyl-5-chloromethylisoxazolines *XXI* formed in high yields (89–93%), and intramolecular cyclization to the pyrrolidone derivatives *XX* did not follow. The chloromethyl derivatives *XXI* are nonreactive, they do not cyclize even if heated in dioxane at 110°C using triethyl-

TABLE I
Photorearrangement quantum yields $\Phi$ (methanol)

| Substituent | *IV*, R = H | *IV*, R = $C_3H_7$ | *XXI*, R = $C_3H_7$ | *IX*[a] |
|---|---|---|---|---|
| H | 0·049 | 0·089 | — | 0·04 |
| 4-$OCH_3$ | 0·012 | 0·022 | — | 0·006 |
| 4-$CH_3$ | 0·026 | 0·060 | 0·005 | 0·016 |
| 4-Cl | — | 0·106 | — | 0·017 |
| 4-F | 0·073 | 0·094 | 0·005 | 0·028 |

[a] In acetonitrile, ref.[15]




SCHEME 4

amine as catalyst or if allowing sodium methoxide to act on them at 80°C for 10 h. In both cases, the unreacted chloro derivatives *XXI* were reclaimed from the mixtures nearly quantitatively. The $\Phi$ values observed for the chloromethyl derivatives *XXIc* and *XXIf* were an order of magnitude lower than those for the corresponding hydroxymethyl derivatives *IV* (Table I).

The attempted synthesis of the 1,3-oxazepin-4-one derivatives *XXII* consisted in the reaction of amide *IVc* with paraformaldehyde in dioxane at boil under the catalytic effect of sulphuric acid. Instead of the expected derivative *XXIIc*, however, 3-(4--methylphenyl)-4-oxo-3*a*,4,6,6*a*-tetrahydrofuro[3,4-*d*]isoxazole (*IIIc*) was isolated in a 99% yield. The reaction of *IVc* with 1,2-dimethoxymethane in dioxane 100°C using methanesulphonic acid as catalyst proceeds in the same manner; instead of the expected reaction with methanol, acid-catalyzed intramolecular cyclization of the starting derivative to the lactone *IIIc* takes place. Amides *IV* cyclize readily to *III* even on the action of boron trifluoride etherate in methanol (*IIIc* in an 80% yield).

## EXPERIMENTAL

The melting temperatures are uncorrected. $^1$H NMR spectra were measured on a Tesla BS 487C instrument, $^{13}$C NMR spectra, on a Jeol JX-60 instrument using dimethyl sulphoxide as solvent; tetramethylsilane served as internal standard. Mass spectra were obtained on a MS 902 S instrument with a direct injection system; ionization energy 70 eV. UV spectra were scanned on a Perkin--Elmer 323 spectrophotometer using thermostatted cells; the substances were measured in methanolic solutions. Absorptivities $\varepsilon$ are in $m^2\ mol^{-1}$.

The photochemical reactions were performed at 20°C using a Toshiba GL-15 15 W low-pressure discharge tube. The reaction vessel was a thermostatted 300 ml photochemical reactor[22] with forced circulation of the reaction solution.

The quantum yields were measured following procedure[23]; the apparatus was as in ref.[24]. The

radiation source was a 6 W low-pressure mercury discharge tube, light intensity $1.49 \cdot 10^{-6}$ mol quant $min^{-1}$ at 253·7 nm; a UV-KSIF 254 interference filter (Carl Zeiss, Jena) was used. The concentrations of the compounds measured were determined from the absorbance decrease at ~265 nm in methanol up to degrees of conversion max. 20%; the optical path length for UV spectral measurements and photolysis was 0·1 cm.

3-Aryl-4-R-carbamoyl-5-hydroxymethylisoxazolines *IVa—IVt*

To a solution of the isoxazoline[16] *III* (25 mmol) in benzene (20 ml) is added a 13% solution of ammonia in methanol (10 ml, 80 mmol) or propylamine (50 mmol) or phenylethylamine (50 mmol or methylamine (15% solution in methanol, 50 mmol) or hydrazine hydrate (50 mmol). The reaction mixture is allowed to stand overnight at room temperature and vacuum evaporated. Pure *IV* is obtained by crystallization of the evaporation residue from acetone.

3-*Phenyl*-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVa). Yield 99%, m.p. 164—166°C. For $C_{11}H_{12}N_2O_3$ (220·2) calculated: 59·99% C, 5·49% H, 12·72% N; found: 60·27% C, 5·32% H, 12·69% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 264 nm (2·99). $^1$H NMR spectrum: 7·25—7·67 (m, 5 H, aromatic-H), 4·99 (t, 1 H, OH), 4·61 (m, 1 H, 5-H), 4·30 (d, $J_{4,5}$ = 6·7 Hz, 1 H, 4-H), 3·50 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 171·01 (s, C=O), 155·02 (s, C=N), 129·81, 129·16, 128·77, 126·43 (aromatic-C), 87·06 (d, $C_{(5)}$), 62·11 (t, $OCH_3$), 55·48 (d, $C_{(4)}$).

3-(4-*Methoxyphenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVb). Yield 97%, m.p. 188 to 191°C. For $C_{12}H_{14}N_2O_4$ (250·2) calculated: 57·59% C, 5·64% H, 11·19% N; found: 57·54% C, 5·81% H, 11·43% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 276 nm (3·11). $^1$H NMR spectrum: 7·81 (bs, 2 H, $NH_2$), 6·84—7·57 (m, 4 H, aromatic-H), 5·00 (t, 1 H, OH), 4·57 (m, 1 H, 5-H), 4·26 (d, $J_{4,5}$ = 7·0 Hz, 1 H, 4-H), 3·70 (s, 3 H, $OCH_3$), 3·47 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 171·01 (s, C=O), 154·40 (s, C=N), 160·42, 127·95, 121·46, 114·15 (aromatic-C), 86·65 (d, $C_{(5)}$), 62·02 (t, $CH_2$), 55·70 (d, $C_{(4)}$).

3-(4-*Methylphenyl*)-4-*carmaboyl*-5-*hydroxymethylisoxazoline* (IVc). Yield 98%, m.p. 201 to 204°C. For $C_{12}H_{14}N_2O_3$ (234·2) calculated: 61·52% C, 6·03% H, 11·96% N; found: 61·80% C, 5·90% H, 11·87% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 270 nm (3·06). $^1$H NMR spectrum: 7·72 (bs, 2 H, $NH_2$), 7·10—7·50 (m, 4 H, aromatic-H), 4·92 (t, 2 H, OH), 4·62 (m, 1 H, 5-H), 4·37 (d, $J_{4,5}$ = 11·0 Hz, 1 H, 4-H), 3·62 (dd, 2 H, $CH_2$), 2·25 (s, 3 H, $CH_3$). $^{13}$C NMR spectrum: 171·19 (s, C=O), 155·93 (s, C=N), 168·15, 139·69, 129·29, 126·18 (aromatic-C), 84·33 (d, $C_{(5)}$), 59·90 (t, $CH_2$), 54·57 (d, $C_{(4)}$).

3-(4-*Chlorophenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVd). Yield 96%, m.p. 221 to 222°C. For $C_{11}H_{11}ClN_2O_3$ (254·7) calculated: 51·87% C, 4·35% H, 11·00% N; found: 52·11% C, 4·17% H, 11·11% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 269 nm (3·13). $^1$H NMR spectrum: 7·780 (bs, 2 H, $NH_2$), 7·27—7·67 (m, aromatic-H), 5·02 (t, 1 H, OH), 4·67 (m, 1 H, 5-H), 4·33 (d, $J_{4,5}$ = = 7·0 Hz, 1 H, 4-H), 3·52 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 170·49 (s, C=O), 155·15 (s C=N), 167·76, 134·36, 128·64, 127·86, 125·39 (aromatic-C), 84·59 (d, $C_{(5)}$), 59·77 (t, $CH_2$), 54·18 (d, $C_{(4)}$).

3-(4-*Fluorophenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVe). Yield 93%, m.p. 163 to 165°C. For $C_{11}H_{11}FN_2O_3$ (238·2) calculated: 55·46% C, 4·65% H, 11·76% N; found: 55·75% C, 4·70% H, 11·55% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 264 nm (3·08). $^1$H NMR spectrum: 7·87 (bs, 2 H, $NH_2$), 7·10—7·75 (m, 4 H, aromatic-H), 5·03 (t, 1 H, OH), 4·66 (m, 1 H, 5-H), 4·33 (d, $J_{4,5}$ = = 7·0 Hz, 1 H, 4-H), 3·52 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 168·17 (s, C=O), 155·31 (s, C=N), 171·15, 128·82, 116·61, 115·18 (aromatic-C), 84·67 (d, $C_{(5)}$), 60·12 (t, $CH_2$), 54·67 (d, $C_{(4)}$).

3-(4-*Bromophenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVf). Yield 95%, m.p. 228–231°C. For $C_{11}H_{11}BrN_2O_3$ (299·1) calculated: 44·16% C, 3·71% H, 9·37% N; found: 43·96% C, 3·44% H, 8·92% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 271 nm (3·19). $^1$H NMR spectrum: 7·87 (bs, 2 H, $NH_2$), 7·25–7·75 (m, 4 H, aromatic-H), 4·98 (t, 1 H, OH), 4·65 (m, 1 H, 5-H), 4·32 (d, $J_{4,5}$ = 7·0 Hz, 1 H, 4-H), 3·55 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 170·62 (s, C=O), 154·12 (s, C=N), 131·64, 128·25, 123·06 (aromatic-C), 87·32 (d, $C_{(5)}$), 61·85 (t, $CH_2$), 55·09 (d, $C_{(4)}$).

3-(2-*Methoxyphenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVg). Yield 96%, m.p. 143 to 145°C. For $C_{12}H_{14}N_2O_4$ (250·2) calculated: 57·59% C, 5·64% H, 11·19% N; found: 57·94% C, 5·76% H, 11·14% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 254 nm (2·71), 286 nm (3·17). $^1$H NMR spectrum: 6·77–7·58 (m, 4 H, aromatic-H), 5·05 (t, 1 H, OH), 4·25–4·92 (m, 2 H, 4-H and 5-H), 3·70 (s, 3 H, $OCH_3$), 3·54 (dd, 2 H, $CH_2$). $^{13}$C NMR spectrum: 170·87 (s, C=O), 154·50 (s, C=N), 156·71, 131·11, 129·03, 120·33, 117·99, 111·88 (aromatic-C), 86·54 (d, $C_{(5)}$), 61·85 (t,$CH_2$), 57·56 (q, $OCH_3$), 55·35 (d, $C_{(4)}$).

3-(2-*Chlorophenyl*)-4-*carbamoyl*-5-*hydroxymethylisoxazoline* (IVh). Yield 94%, m.p. 147–149°C, For $C_{11}H_{11}ClN_2O_3$ (254·7) calculated: 51·87% C, 4·35% H, 11·00% N; found: 51·83% C, 4·43% H. 11·28% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 248 nm (2·80). $^1$H NMR spectrum: 7·18–7·60 (m, 4 H, aromatic-H), 4·77 (m, 1 H, 5-H), 4·62 (d, $J_{4,5}$ = 8·0 Hz, 1 H, 4-H), 3·57 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 169·73 (t, C=O), 154·40 (s, C=N), 156·61, 131·81, 131·03, 130·12, 128·04, 127·13 (aromatic-C), 86·74 (d, $C_{(5)}$), 61·68 (t, $CH_2$), 57·52 (d, $C_{(4)}$).

3-*Phenyl*-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVi). Yield 99%, m.p. 167–169°C. For $C_{14}H_{18}N_2O_3$ (262·3) calculated: 64·10% C, 6·92% H, 10·68% N; found: 64·32% C, 6·84% H, 10·81% N. $^1$H NMR spectrum: 8·39 (t, 1 H, NH), 7·29–7·57 (m, 5 H, aromatic-H), 4·37–4·82 (m, 2 H, 4-H, 5-H), 3·59 (dd, 2 H, $OCH_2$), 2·92 (m, 2 H, $CH_2$), 1·30 (m, 2 H, $CH_2$), 0·72 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 165·94 (s, C=O), 155·93 (s, C=N), 129·81, 129·16, 128·64, 126·04 (aromatic-C), 84·46 (d, $C_{(5)}$), 59·90 (t, $OCH_2$), 54·70 (d, $C_{(4)}$), 40·54 (t, $CH_2$), 21·96 (t, $CH_2$), 11·17 (q, $CH_3$).

3-(4-*Methoxyphenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVj). Yield 93%, m.p. 185–187°C. For $C_{15}H_{20}N_2O_4$ (292·3) calculated: 61·33% C, 6·90% H, 9·58% N; found: 61·33% C, 6·80% H, 7·54% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 279 nm (3.17). $^1$H NMR spectrum: 8·30 and 4·92 (t, t, 2 H, OH, NH), 6·87–7·54 (m, 4 H, aromatic-H), 4·61 (m, 1 H, 5-H), 4·40 (d, $J_{4,5}$ = 11 Hz, 1 H, 4-H), 3·64 (dd, 2 H, $CH_2O$), 3·75 (s, 3 H, $OCH_3$), 2·96 (m, 2 H, $CH_2$), 1·35 (m, 2 H, $CH_2$), 0·78 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 166·07 (s, C=O), 155·54 (s, C=N), 160·48, 127·73, 121·63, 114·22 (aromatic-C), 84·20 (d, $C_{(5)}$), 60·03 (t, $CH_2$), 55·09 (d, $C_{(4)}$), 22·09 (t, $CH_2$), 11·30 (q, $CH_3$).

3-(4-*Methylphenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVk). Yield 97%, m.p. 179–180°C. For $C_{15}H_{20}N_2O_3$ (276·3) calculated: 65·19% C, 7·30% H, 10·14% N; found: 65·02% C, 7·29% H, 10·01% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 268 nm (3·13). $^1$H NMR spectrum: 8·32 and 4·98 (t, t, 2 H, NH, OH). 7·15–7·51 (m, 4 H, aromatic-H), 4·65 (m, 1 H, 5-H), 4·45 (d, $J_{4,5}$ = 10 Hz, 1 H, 4-H), 3·63 (dd, 2 H, $OCH_2$), 2·92 (m, 2 H, $CH_2$), 2·30 (s, 3 H, $CH_3$), $^{13}$C NMR spectrum: 165·96 (s, C=O), 155·83 (s, C=N), 139·73, 129·34 ,126·22 (aromatic-C), 84·41 (d, $C_{(5)}$), 59·99 (t, $OCH_2$), 54·93 (d, $C_{(4)}$), 22·20 (t, $CH_2$), 21·03 (q, $CH_3$), 11·42 (q, $CH_3$).

3-(4-*Chlorophenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVl). Yield 91%, m.p. 194–196°C. For $C_{14}H_{17}ClN_2O_3$ (296·7) calculated: 56·66% C, 5·77% H, 9·44% N; found: 56·47% C, 5·78% H, 9·40% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 270 nm (3·12). IR spectrum: 1 645 $cm^{-1}$ (C=O). $^1$H NMR spectrum: 8·42 (m, 1 H, NH), 7·51–7·61 (m, 4 H, aromatic-H), 5·27 (t, 1 H, OH), 4·75 (m, 1 H, 5-H), 4·51 (d, $J_{4,5}$ = 10 Hz, 1 H, 4-H), 3·64 (dd, 2 H, $OCH_2$), 3·02 (m, 2 H, $CH_2$), 1·41 (m, 2 H, $CH_2$), 0·83 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 166·20 (s, C=O), 155·67

(s, C=N), 135·01, 129·16, 128·25 (aromatic-C), 84·98 (d, $C_{(5)}$), 60·16 (t, $CH_2O$), 54·83 (d, $C_{(4)}$), 22·35 (t, $CH_2$), 11·56 (q, $CH_3$).

3-(4-*Fluorophenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVm). Yield 97%, m.p. 185–186°C. For $C_{14}H_{17}FN_2O_3$ (280·3) calculated: 59·98% C, 6·11% H, 9·99% N; found: 59·86% C, 6·20% H, 9·77% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 267 nm (3·03). $^1$H NMR spectrum: 8·43 (s, 1 H, NH), 7·19–7·77 (m, 4 H, aromatic-H), 5·15 (t, 1 H, OH), 4·70 (m, 1 H, 5-H), 4·42 (d, $J_{4,5}$ = 8 Hz, 1 H, 4-H), 3·62 (dd, 2 H, $OCH_2$), 3·03 (m, 2 H, $CH_2$), 1·41 (m, 2 H, $CH_2$), 0·81 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 165·94 (s, C=O), 155·28 (s, C=N), 128·78, 128·26, 126·05, 116·69, 115·26 (aromatic-C), 84·72 (d, $C_{(5)}$), 59·91 (t, $OCH_2$), 54·83 (d, $C_{(4)}$), 22·22 (t, $CH_2$), 11·43 (q, $CH_3$).

3-(4-*Bromophenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVn). Yield 96%, m.p. 168–169°C. For $C_{14}H_{17}BrN_2O_3$ (341·2) calculated: 49·28% C, 5·02% H, 8·21% N; found: 49·57% C, 5·19% H, 8·50% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 272 nm (3·10). $^1$H NMR spectrum: 8·30 (m, 1 H, NH), 7·38–7·65 (m, 4 H, aromatic-H), 4·96 (t, 1 H, OH), 4·67 (m, 1 H, 5-H), 4·47 (d, $J_{4,5}$ = 11 Hz, 1 H, 4-H), 3·60 (dd, 2 H, $OCH_2$), 2·96 (m, 2 H, $CH_2$), 1·35 (m, 2 H, $CH_2$), 0·78 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 165·98 (s, C=O), 155·51 (s, C=N), 131·99, 128·54, 128·30, 123·45 (aromatic-C), 84·95 (d, $C_{(5)}$), 60·03 (t, $OCH_2$), 54·71 (d, $C_{(4)}$), 40·78 (t, $CH_2$), 22·24 t, $CH_2$), 11·53 (q, $CH_3$).

1 3-(4-*Nitrophenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVo). Yield 91%, m.p. 182 to 584°C. For $C_{14}H_{17}N_3O_5$ (307·3) calculated: 54·72% C, 5·58% H, 13·67% N; found: 54·42% C, (·50% H, 13·39% N. UV spectrum ,$\lambda_{max}$ (log $\varepsilon$): 308 nm (3·02). IR spectrum: 1 638 cm$^{-1}$ (C=O). Mass spectrum, *m/z*: 307 ($M^+$), 191 (base peak). $^1$H NMR spectrum: 8·56 (m, 1 H, NH), 7·83 to 8·32 (m, 4 H, aromatic-H), 5·16 (t, 1 H, OH), 4·77 (m, 1 H, 5-H), 4·50 (d, $J_{4,5}$ = 7 Hz, 1 H, 4-H), 3·62 (dd, 2 H, $OCH_2$), 3·02 (m, 2 H, $CH_2$), 1·33 (m, 2 H, $CH_2$), 0·79 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 168·30 (s, C=O), 154·14 (s, C=N), 147·91, 135·31, 127·39, 124·02 (aromatic-C), 88·17 (d, $C_{(5)}$), 61·94 (t, $OCH_2$), 55·06 (d, $C_{(4)}$), 22·20 (t, $CH_2$), 11·42 (q, $CH_3$).

3-(3-*Nitrophenyl*)-4-*propylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVp). Yield 93%, m.p. 151 to 153°C. For $C_{14}H_{17}N_3O_5$ (307·3) calculated: 54·72% C, 5·58% H, 13·67% N; found: 54·47% C, 5·61% H, 13·45% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 260 nm (3·08). $^1$H NMR spectrum: 8·58 (m, 1 H, NH), 7·30–7·73 (m, 4 H, aromatic-H), 5·10 (t, 1 H, OH), 4·60–4·97 (m, 2 H, 4-H and 5-H), 3·67 (dd, 2 H, $OCH_2$), 3·00 (m, 2 H, $CH_2$), 1·44 (m, 2 H, $CH_2$), 0·81 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 165·68 (s, C=O), 154·89 (s, C=N), 148·01, 132·28, 130·85, 130·59, 124·36, 120·46 (aromatic-C), 85·24 d, $C_{(5)}$), 59·77 (t, $CH_2$), 54·44 (d, $C_{(4)}$), 21·96 (t, $CH_2$), 11·30 (q, $CH_3$).

3-*Phenyl*-4-(2-*phenylethyl*)*carbamoyl*-5-*hydroxymethylisoxazoline* (IVr). Yield 95%, m.p. 148 to 150°C. For $C_{19}H_{20}N_2O_4$ (324·4) calculated: 70·35% C, 6·21% H, 8·63% N; found: 70·49% C, 6·09% H, 8·79% N. $^1$H NMR spectrum: 7·22–7·50 (m, 5 H, aromatic-H), 7·14 (s, 5 H, aromatic--H), 4·30–4·79 (m, 2 H, 4-H and 5-H), 3·90 (bs, 1 H, OH), 3·52 (dd, 2 H, $OCH_2$), 3·21 (m, 2 H, $CH_2$), 2·61 (m, 2 H, $CH_2$). $^{13}$C NMR spectrum: 165·94 (s, C=O), 155·80 (s, C=N), 139·04, 129·68, 129·03, 128·51, 126·04 (aromatic-C), 84·46 (d, $C_{(5)}$), 59·77 (t, $OCH_2$), 54·57 (d, $C_{(4)}$).

3-(4-*Methoxyphenyl*)-4-(2-*phenylethyl*)*carbamoyl*-5-*hydroxymethylisoxazoline* (IVs). Yield 91%, m.p. 168–169°C. For $C_{20}H_{22}N_2O_4$ (354·4) calculated: 67·77% C, 6·26% H, 7·91% N; found: 67·50% C, 6·11% H, 8·18% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 278 nm (3·16). $^1$H NMR spectrum: 8·34 (bs, 1 H, NH), 6·78–7·44 (m, 4 H, aromatic-H), 7·68 (s, 5 H, aromatic-H), 4·88 (t, 1 H, OH), 4·55 (m, 1 H, 5-H), 4·33 (d, $J_{4,5}$ = 10 Hz), 1 H, 4-H), 3·70 (s, 3 H, $OCH_3$), 3·52 (dd, 2 H, $OCH_2$), 3·23 (m, 2 H, $CH_2$), 2·67 (m, 2 H, $CH_2$). $^{13}$C NMR spectrum: 166·20 (s, C=O), 155·41 (s, C=N), 160·48, 139·30, 128·64, 127·73, 121·63, 114·22 (aromatic-C), 84·20 (d, $C_{(5)}$), 59·77 (t, $OCH_2$), 54·83 and 55·22 (d, q, $C_{(4)}$, $OCH_3$).

3-(4-*Fluorophenyl*)-4-*methylcarbamoyl*-5-*hydroxymethylisoxazoline* (IVt). Yield 92%, m.p. 135–137°C. For $C_{12}H_{13}FN_2O_3$ (252·2) calculated: 57·14% C, 5·19% H, 11·11% N; found: 57·29% C, 5·27% H, 10·94% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 262 nm (2·96). $^1$H NMR spectrum: 8·25 (m, 1 H, NH), 7·07–7·62 (m, 4 H, aromatic-H), 5·16 (t, 1 H, OH), 4·60 (m, 1 H, 5-H), 4·90 (d, $J_{4,5}$ = 7 Hz, 1 H, 4-H), 3·50 (dd, 2 H, $OCH_2$).

3-*Phenyl*-4-*aminocarbamoyl*-5-*hydroxymethylisoxazoline* (Va). Yield 80%, m.p. 189–191°C. For $C_{11}H_{13}N_3O_3$ (235·2) calculated: 56·16% C, 5·57% H, 17·86% N; found: 56·09% C, 5·58% H, 18·03% N. $^1$H NMR spectrum: 9·53 (bs, 1 H, NH), 7·25–7·60 (m, 5 H, aromatic-H), 4·98 (t, 1 H, OH), 4·58 (m, 1 H, 5 H), 4·25 (d, $J_{4,5}$ = 6·7 Hz, 1 H, 4-H), 3·47 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 168·02 (s, C=O), 154·50 (s, C=N), 129·81, 128·64, 126·30 (aromatic-C), 86·54 (d, $C_{(5)}$), 61·85 (t, $OCH_2$), 53·79 (d, $C_{(4)}$).

3-(4-*Methoxyphenyl*)-4-*aminocarbamoyl*-5-*hydroxymethylisoxazoline* (Vb). Yield 91%, m.p. 193–195°C. For $C_{12}H_{15}N_3O_4$ (265·3) calculated: 54·33% C, 5·70% H, 15·84% N; found: 54·82% C, 5·59% H, 15·93% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 277 nm (3·11). $^1$H NMR spectrum: 10·3 (bs, 1 H, NH), 7·55–6·87 (m, 4 H, aromatic-H), 4·71 (m, 1 H, 5 H), 4·68 (d, $J_{4,5}$ = 10 Hz, 1 H, 4-H), 3·60 (dd, 2 H, $OCH_2$), 3·70 (s, 3 H, $CH_3O$). $^{13}$C NMR spectrum: 168·88 (s, C=O), 155·72 (s, C=N), 160·80, 128·12, 121·74, 114·45 (aromatic-C), 84·37 (d, $C_{(5)}$), 59·89 (t, $OCH_2$), 55·33 and 53·64 (q, d, $C_{(4)}$ and $CH_3O$).

3-(4-*Bromophenyl*)-4-*aminocarbamoyl*-5-*hydroxymethylisoxazoline* (Vf). Yield 93%, m.p. 187 to 190°C. For $C_{11}H_{12}BrN_3O_3$ (314·1) calculated: 42·05% C, 3·85% H, 13·37% N; found: 42·25% C, 3·84% H, 13·30% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 272 nm (3·22). $^1$H NMR spectrum: 9·46 (bs, 1 H, NH), 7·68–7·44 (m, 4 H, aromatic-H), 5·07 (t, 1 H, OH), 4·71 (m, 1 H, 5-H), 4·44 (d, $J_{4,5}$ = 10·5 Hz, 1 H, 4-H), 3·64 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 165·16 (s, C=O), 154·89 (s, C=N), 131·63, 127·99, 122·93 (aromatic-C), 84·59 (s, $C_{(5)}$), 59·64 (t, $OCH_2$), 52·62 (d, $C_{(4)}$).

3-(2-*Fluorophenyl*)-4-*aminocarbamoyl*-5-*hydroxymethylisoxazoline* (Vj). Yield 90%, m.p. 168 to 171°C. For $C_{11}H_{12}FN_3O_3$ (253·2) calculated: 52·17% C, 4·78% H, 16·59% N; found: 51·81% C, 4·63% H, 16·40% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 272 nm (3·14). $^1$H NMR spectrum: 9·45 (bs, 1 H, NH), 7·45–7·69 (m, 4 H, aromatic-H), 5·02 (t, 1 H, OH), 4·71 (m, 1 H, 5-H), 4·43 (d, $J_{4,5}$ = 11 Hz, 1 H, 4-H), 3·63 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 165·16 (s, C=O), 154·89 (s, C=N), 131·63, 127·99, 123·06 (aromatic-C), 84·59 (d, $C_{(5)}$), 59·64 (t, $OCH_2$), 52·62 (d, $C_{(4)}$).

Photorearrangement of Isoxazolines *IVa–IVe* to *Z*-2-Hydroxymethylamino-2-aryl-1-formylacrylamides

Solution of isoxazoline (2 mmol) in methanol (300 ml) is irradiated until the starting substance is undetectable by thin layer chromatography. The reaction mixture is vacuum concentrated and the crude product *VI* is obtained by trituration of the residue with methanol (5 ml) and collected by filtration. The pure product is crystallized from methanol.

*Z*-2-*Hydroxymethylamino*-2-*phenyl*-2-*formylacrylamide* (VIa). Irradiation time 6 h, yield 75%, m.p. 125–127°C. For $C_{11}H_{12}N_2O_3$ (220·2) calculated: 59·99% C, 5·49% H, 12·72% N; found: 59·87% C, 5·41% H, 12·99% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 240 nm (2·97), 284 nm (3·11). $^1$H NMR spectrum: 8·83 (t, 1 H, NH), 8·49 (s, 1 H, CHO), 7·29–7·51 (m, 5 H, aromatic-H), 6·07 (t, 1 H, OH), 4·27 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 188·16 (d, COH), 174·53 (s, C=O), 170·24 (s, C–C), 130·12, 128·56 (aromatic-C), 102·46 (s, C=C), 67·39 (t, $OCH_2$).

*Z*-2-*Hydroxymethylamino*-2-(4-*methoxyphenyl*)-1-*formylacrylamide* (VIb). Irradiation time 7·5 h, yield 67%, m.p. 171–172°C. For $C_{12}H_{14}N_2O_4$ (250·2) calculated: 57·59% C, 5·64% H, 11·19% N; found: 57·29% C, 5·49% H, 11·43% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 244 nm (2·88),

291 nm (3·12). $^1$H NMR spectrum: 8·87 (m, 1 H, NH), 8·56 (s, 1 H, CHO), 6·96–7·33 (m, 4 H, aromatic-H), 4·35 (dd, 2 H, $OCH_2$), 3·77 (s, 3 H, $OCH_3$). $^{13}$C NMR spectrum: 188·42 (d, CHO), 174·65 (s, C=O), 170·37 (s, C=C), 160·37, 130·25, 127·78, 122·06, 113·88 (aromatic-C), 102·59 (s, C=C), 67·39 (t, $OCH_2$), 55·32 (q, $OCH_3$).

*Z*-2-*Hydroxymethylamino*-2-(4-*methylphenyl*)-1-*formylacrylamide* (VIc). Irradiation time 8·5 h, yield 81%, m.p. 237–240°C. For $C_{12}H_{14}N_2O_3$ (234·2) calculated: 61·52% C, 6·02% H, 11·96% N; found: 61·60% C, 5·94% H, 11·56% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 244 nm (3·01), 284 nm (3·06). Mass spectrum, *m/z*: 234 ($M^+$), 159 (base peak). $^1$H NMR spectrum: 8·83 (m, 1 H, NH), 8·53 (s, 1 H, CHO), 7·25 (s, 4 H, aromatic-H), 6·07 (t, 1 H, OH), 4·31 (dd, 2 H, $OCH_2$), 2·32 (s, 3 H, $CH_3$). $^{13}$C NMR spectrum: 188·29 (d, CHO), 174·77 (s, C=O), 170·23 (s, C=C), 139·56, 128·90, 128·51, 127·21 (aromatic-C), 102·30 (s, C=C), 67·31 (t, $OCH_2$), 20·79 (q, $CH_3$).

*Z*-2-*Hydroxymethylamino*-2-(4-*chlorophenyl*)-1-*formylacrylamide* (VId). Irradiation time 6 h, yield 67%, m.p. 168–170°C. For $C_{11}H_{11}ClN_2O_3$ (254·7) calculated: 57·87% C, 4·35% H, 11·00% N; found: 51·71% C, 4·29% H, 11·36% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 244 nm (2·71), 288 nm (2·58). $^1$H NMR spectrum: 8·80 (m, 1 H, NH), 8·51 (s, 1 H, CHO), 7·43–7·61 (m, 4 H, aromatic-H), 6·11 (t, 1 H, OH), 4·30 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 188·02 (d, CHO), 173·47 (s, C=O), 170·10 (s, C=C), 134·75, 130·46, 128·51, 127·56 (aromatic-C), 102·52 (s, C=C), 67·18 (t, $OCH_2$).

Standing in solution (dimethyl sulphoxide or methanol, 30 days), *VId* isomerizes to *E*-2-hydroxymethylamino-2-(4-chlorophenyl)-1-formylacrylamide (*XXIIId*). $^1$H NMR spectrum: 8·75 (s, 1 H, CHO), 7·43–7·61 (m, 4 H, aromatic-H), 5·76 (t, 1 H, OH), 4·58 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 188·16 (d, CHO), 174·65 (s, C=O), 170·35 (s, C=C), 168·41, 135·53, 130·72, 128·90, 128·25 (aromatic-C), 102·00 (s, C=C), 67·44 (t, $OCH_2$).

*Z*-2-*Hydroxymethylamino*-2-(4-*fluorophenyl*)-1-*formylacrylamide* (VIe). Irradiation time 6 h, yield 69%, m.p. 113–115°C. For $C_{11}H_{11}FN_2O_2$ (238·2) calculated: 55·46% C, 4·65% H, 11·76% N, found: 55·54% C, 4·50% H, 11·74% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 244 nm (2·89), 288 nm (2·88). $^1$H NMR spectrum: 8·66 (s, 1 H, CHO), 7·25–7·62 (m, 4 H, aromatic-H). 4·57 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 188·29 (d, CHO), 173·87 (s, C=O), 170·37 (s, C=C), 167·91, 131·54, 130·90, 126·61, 115·05 (aromatic-C), 102·85 (s, C=C), 67·39 (t, $OCH_2$).

Standing in solution (dimethyl sulphoxide or methanol, 30 days), *VIe* isomerizes to *E*-2-hydroxymethylamino-2-(4-fluorophenyl)-1-formylacrylamide (*XXIIIe*). $^1$H NMR spectrum: 8·75 (s, 1 H, CHO), 7·26–7·60 (m, 4 H, aromatic-H), 4·31 (dd, 2 H, $OCH_2$). $^{13}$C NMR spectrum: 187·76 (d, CHO), 174·39 (s, C=O), 169·97 (s, C=C), 163·23, 130·72, 130·51, 126·61, 114·27 (aromatic-C). 101·94 (s, C=C), 64·93 (t, $OCH_2$).

Reaction of *IV* with Thionyl Chloride

A mixture of *IV* (10 mmol) with thionyl chloride (1 ml) in benzene (20 ml) is heated in an autoclave at 90°C for 2·5 h. The crystals of *XXI* obtained are filtered out and crystallized from acetone. Additional fraction of product is obtained by concentrating the filtrate by evaporation.

3-(4-*Methylphenyl*)-4-*propylcarbamoyl*-5-chloromethylisoxazoline (XXIc). Yield 93%, m.p. 165–166°C. For $C_{15}H_{19}ClN_2O_2$ (294·7) calculated: 61·12% C, 6·50% H, 9·51% N; found: 60·81% C, 6·32% H, 9·67% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 279 nm (3·15). IR spectrum: 1 647 $cm^{-1}$ (C=O). $^1$H NMR spectrum: 8·50 (m, 1 H, NH ), 7·12–7·56 (m, 4 H, aromatic-H), 4·87 (m, 1 H, 5-H), 4·40 (d, $J_{4,5}$ = 6 Hz, 1 H, 4-H), 3·82 (d, $J$ = 5 Hz, 2 H, $CH_2Cl$), 2·91 (m, 2 H, $CH_2$), 1·31 (m, 2 H, $CH_2$), 0·73 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 167·89 (s, C=O), 154·89 (s, C=N), 139·82, 129·16, 126·43, 125·66 (aromatic-C), 84·33 (d, $C_{(5)}$), 57·30 (d, $C_{(4)}$), 45·61 (t, $CH_2Cl$), 21·96 (t, $CH_2$), 20·79 (q, $CH_3$), 11·17 (q, $CH_3$).

3-(4-*Chlorophenyl*)-4-*propylcarbamoyl*-5-*chloromethylisoxazoline* (XXId). Yield 90%, m.p. 194–196°C. For $C_{14}H_{16}Cl_2N_2O_2$ (315·2) calculated: 53·74% C, 5·19% H, 9·05% N; found: 53·34% C, 5·12% H, 8·89% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 269 nm (3·01). $^1$H NMR spectrum: 8·50 (m, 1 H, NH), 7·37–7·65 (m, 4 H, aromatic-H). 4·43–5·05 (m, 2 H, 4-H and 4-H), 3·76 (m, 2 H, $CH_2Cl$), 2·96 (m, 2 H, $CH_2$), 1·33 (m, 2 H, $CH_2$), 0·75 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 165·49 (s, C=O), 155·98 (s, C=N), 135·15, 129·16, 125·38 (aromatic-C), 83·46 (d, $C_{(5)}$), 55·46 (d, $C_{(4)}$), 22·00 (t, $CH_2$), 11·32 (q, $CH_3$).

3-(4-*Fluorophenyl*)-4-*propylcarbamoyl*-5-*chloromethylisoxazoline* (XXIe). Yield 89%, m.p. 177–179°C. For $C_{14}H_{16}FClN_2O_2$ (298·7) calculated: 56·28% C, 5·40% H, 9·38% N; found: 55·61% C, 5·24% H, 9·62% N. UV spectrum, $\lambda_{max}$ (log $\varepsilon$): 262 nm (3·03). IR spectrum: 1 645 $cm^{-1}$ (C=O). Mass spectrum, *m/z*: 300, 298 ($M^{\ddagger}$), 262 ($M^{\ddagger}$-HCl), 164 (base peak). $^1$H NMR spectrum: 8·50 (m, 1 H, NH), 7·11–7·63 (m, 4 H, aromatic-H), 4·92 (m, 1 H, 5-H), 4·43 (d, $J_{4,5}$ = 6 Hz, 1 H, 4-H), 3·85 (d, $J$ = 5 Hz, 2 H, $CH_2Cl$), 2·96 (m, 2 H, $CH_2$), 1·31 (m, 2 H, $CH_2$), 0·71 (t, 3 H, $CH_3$). $^{13}$C NMR spectrum: 167·76 (s, C=O), 161·00, 129·16, 128·64, 116·56, 115·13, (aromatic-C), 84·72 (d, $C_{(5)}$), 57·30 (d, $C_{(4)}$), 45·74 (t, $CH_2Cl$), 32·09 (t, $CH_2$), 21·96 (t, $CH_2$), 11·30 (q, $CH_3$).

Attempted Cyclization of *IVc* to *XXII* with Formaldehyde

A mixture of *IVc* (2·3 g, 10 mmol), paraformaldehyde (1 g), dry dioxane (20 ml) and concentrated sulphuric acid (0·04 ml) was heated for 15 h at the solvent boiling temperature. After vacuum concentration, the residue was crystallized to obtain 3-(4-methylphenyl)-4-oxo-3*a*,4,6,6*a*-tetrahydrofuro[3,4-*d*]isoxazole (*IIIc*) in a 99% yield; m.p. 155–157°C (ref.[16], 155–157°C).

Intramolecular Alcoholysis of Amide *IVc*

A mixture of *IVc* (0·23 g, 1 mmol) and two drops of boron trifluoride etherate in methanol (30 ml) was stirred at room temperature for 40 h. Working-up as above gave *IIIc* in a 80% yield.

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