PHOTO-INDUCED REARRANGEMENT OF ISOXAZOLINES — A PATHWAY TO 2,4,5,8-TETRAHYDRO-1,3-DIOXA-5-AZOCINE DERIVATIVES

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Dedicated to Prof. R. Huisgen on the occasion of his 65th birthday.

4-R-Substituted-8-X-phenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-enes (X = H, 4-CH_3, 4-OCH_3, 4-Cl, 4-Br, 4-F, 3-NO_2, 3-Cl, 3-Br) have been prepared by cycloaddition of substituted benzenenitriloxides with 2-R-substituted 1,3-dioxep-5-enes (R = H, CH_3, C_6H_5). A mixture of the *endo* and *exo* adducts is formed, if R is CH_3 or C_6H_5. Their irradiation produces high yields of the title compounds as the single products. High selectivity of the photo-rearrangement is due to resonance stabilization of the biradical with *p* electrons of the oxygen atom. The quantum yields of the photoreaction vary from 0·02 to 0·04 depending on the substituent X. An unexpected dependence has been found between the quantum yield of the photo-rearrangement and stereochemical arrangement of the 4-R-substituent: *exo* derivatives exhibit higher values than the *endo* derivatives. Also different are UV spectra of the *endo* and *exo* derivatives. A new synthesis principle is described enabling preparation of $(n + 1)$-membered heterocycles from *n*-membered heterocycles.

Photo-induced rearrangements of isoxazoline derivatives usually have non-selective course[1-9]. Recently we have found[10-12] that introduction of a structural element which stabilizes the biradical formed by an overlap with *p* electrons of oxygen atom results in unusual selectivity of the photo-induced rearrangement giving heterocyclic enaminoaldehydes *I*→*II*. The aim of this work was to verify the concept proposed by a further variation of heterocycle. Therefore, we prepared isoxazolines condensed with seven-membered 1,3-dioxepane skeleton.

High yields of 4-R-substituted-8-phenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-enes (*IVa*–*IVe*) were prepared by reaction of benzenehydroximic acid chloride with 2-R-substituted 1,3-dioxep-5-enes (*III*, *R* = H, CH_3, C_6H_5) in ether solution in the presence of triethylamine (method A). The formation of 3,5,10-trioxa-9-aza-

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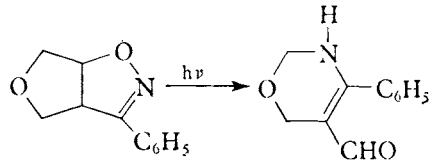
bicyclo[5,3,0]dec-8-ene represents the first case of 1,3-dipolar cycloaddition of 1,3--dioxep-5-ene derivatives. Structure of the parent compound *IVa* was proved by both ^{1}H NMR (the presence of doublets of the bridge-head protons at 4·88 ppm (1-H) and 4·63 ppm (7-H) with the coupling constant $J_{1-7} = 6·0$ Hz, confirming the *cis* stereospecificity of the concerted 1,3-dipolar cycloaddition) and ^{13}C NMR spectra (the presence of a singlet at 158·28 ppm (C=N) and doublets at 84·41 ppm ($C_{(1)}$) and 52·89 ppm ($C_{(7)}$)). The bent structure of the bicyclic system *IVa* causes unequal values of chemical shifts of the triplets of $C_{(2)}$ (17·28 ppm) and $C_{(6)}$ (68·61 ppm). The higher value of $C_{(2)}$ was ascribed with respect to the greater effect of the isoxazoline oxygen atom.

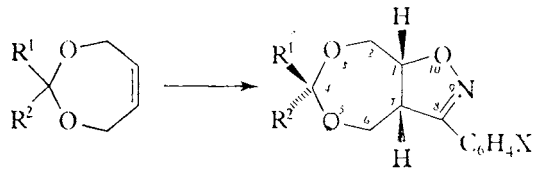
The 1,3-dipolar cycloaddition of benzenenitriloxide to 2-phenyl- or 2-methyl--1,3-dioxep-5-ene exhibits *endo-exo* stereoselectivity: it produces a diastereoisomeric pair of the *endo* adduct with *anti* arrangement of the bridge-head isoxazoline protons 1-H and 7-H with the 4-H proton at the chiral centre (the adducts *IVb* and *IVd*, respectively) and the *exo* adduct with *syn* arrangement of the said proton (the adducts *IVc* and *IVe*, respectively). The *endo-exo* stereoselectivity relates to the 2-R--substituent in the heterocyclic dipolarophile. Scheme 1 gives the chair conformations with *cis* arrangement of the bridge-head protons of the derivatives *IV* "*endo*" and *IV* "*exo*". The other conceivable stereochemical arrangement of the bicyclic system with *trans* arrangement of the bridge-head protons can be excluded with respect to the pure *cis* stereospecificity of the 1,3-dipolar cycloaddition of nitriloxides. With respect to the torsion strain the boat conformation *XII* is not considered either. The ratio is *endo* : *exo* = 9 : 4 and 7 : 1 for the 4-phenyl- and 4-methylsubstituted derivatives, respectively, *i.e.* in favour of the sterically more advantageous *endo* adducts. The *endo* and *exo* diastereoisomers could be separated by column chromatography, and their structures were assigned on the basis of different chemical shifts (due to the bent structure of the bicyclic adducts formed) of the $C_{(2)}$ and $C_{(6)}$ triplets in their ^{13}C NMR spectra. Due to equatorial arrangement of the substituent, the *endo* adducts *IVb* and *IVd* have the said signals at approximately the same δ values as the non-substituted derivative *IVa*; for *IVb* δ 70·90 ppm ($C_{(2)}$) and 66·90 ppm ($C_{(6)}$), for *IVd* δ 70·43 ppm ($C_{(2)}$) and 66·66 ppm ($C_{(6)}$). The γ effect is observed in the ^{13}C NMR spectra of the *exo* adducts: the respective triplets are shifted upfield, which is due to the effect of the axial 4-R substituent. For *IVc* δ 65·68 ppm ($C_{(2)}$) and 63·93 ppm ($C_{(6)}$), for *IVe* δ 66·21 ppm ($C_{(2)}$) and 64·71 ppm ($C_{(6)}$).

Different values are also observed for the $C_{(4)}$ atom which carries the substituent as well as for the signals of 4-H atom. The values of signals of the isoxazoline C atoms do not show any significant differences. Analogous results were also obtained from the 1,3-dipolar cycloaddition of 9-anthracenenitriloxide with the above-mentioned dipolarophiles. The *endo* and *exo* adducts were obtained in this case, too[13]. It is, however, surprizing to find that values of their longest-wave maxima in UV spectra and their character are also different. The *endo* adducts *IVb* and *IVd* have

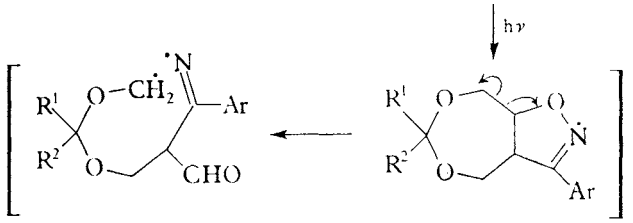
the λ_{max} values 260 and 261 nm, respectively, the *exo* adducts *IVc* and *IVe* have the λ_{max} values 266 and 265 nm, respectively; moreover, the *exo* adducts differ from the *endo* adducts (and from *IVa*, too) by the presence of another absorption band at lower wavelengths.



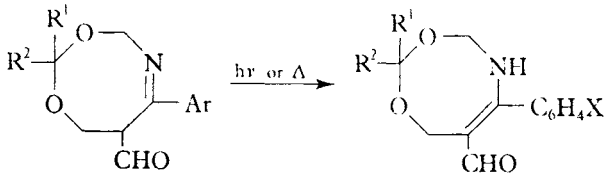
I *II*



III *IV*



VI, Ar = C_6H_4X *V*, Ar = C_6H_4X



VII *VIII*

In Formulae *III*—*VIII*: *a*, $R^1 = R^2 = H$, X = H; *b*, $R^1 = C_6H_5$, $R^2 = H$, X = H; *c*, $R^1 = H$, $R^2 = C_6H_5$, X = H; *d*, $R^1 = CH_3$, $R^2 = H$, X = H; *e*, $R^1 = H$, $R^2 = CH_3$, X = H; *f*, $R^1 = R^2 = H$, X = 4-F; *g*, $R^1 = R^2 = H$, X = 4-Cl; *h*, $R^1 = R^3 = H$, X = 4-Br; *i*, $R^1 = R^2 = H$, X = 4-CH_3; *j*, $R^1 = R^2 = H$, X = 3-OCH_3; *k*, $R^1 = R^2 = H$, X = 3-NO_2; *l*, $R^1 = R^2 = H$, X = 3-Cl; *m*, $R^1 = R^2 = H$, X = 3-Br.

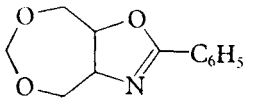
The 8-(2-phenyl)substituted 3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-enes were prepared either from the respective benzhydroximic acid chlorides (method *A*) (for X = = 4-F (*IVf*), 4-Cl (*IVg*), 4-Br (*IVh*), 3-NO_3 (*IVk*), 3-Cl (*IVl*), and 3-Br (*IVm*)) or by the method recently published[14] in which the corresponding nitriloxides are obtained by action of sodium hypochlorite on the substituted benzaldoximes (method B) (X = 4-CH_3 (*IVi*) and 4-OCH_3 (*IVj*)). Structures were assigned to the derivatives *IVf*–*IVk* as in the case of the *IVa* derivative.

The preparative photo-reaction was accomplished by irradiation with monochromatic radiation with λ_{max} = 253·7 nm. The photolysis of the acetonitrile solution of compound *IVa* gave a product exhibiting the molecular peak $M^{\ddagger}$ *m/z* 219 in its mass spectrum, which indicates the rearrangement product. Out of the structures conceivable on the basis of available findings[11], we assigned the structure of 6-phenyl-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIa*) to the product obtained on the basis of interpretation of spectral data. The ^{1}H NMR spectrum contains a singlet at 8·89 ppm due to the aldehydic proton; position of this singlet does not change on heating or on addition of ^2H_2O. The ^{13}C NMR spectrum contains signals of singlets at 162·82 and 110·71 ppm (due to carbon atoms of the double bond of the enaminoaldehyde structural unit) as well as a signal of doublet at 188·57 ppm (due to the aldehydic carbon atom). The longest-wave absorption maximum at 296 nm in the UV spectrum shows a bathochromic shift as compared with *IVa*, which is due to the —NH—C=C—CHO and C_6H_5—C=C—CHO chromophors. The ^{1}H NMR spectrum of *VIIIa* contains a sharp singlet at 4·91 ppm due to the 2-H atom adjacent to two oxygen atoms which does not change its multiplicity in various solvents. The two protons at $C_{(2)}$ absorb as singlets, one at 4·91 ppm and the other at 4·79 ppm. The absence of geminal coupling constant from the eight-membered heterocyclic ring of 2,4,5,8-tetrahydro-1,3-dioxa-5-azocine represents an interesting finding with regard to other smaller cyclic systems[15]. The Dreiding model of compound *VIIIa* exhibits a high degree of flexibility.

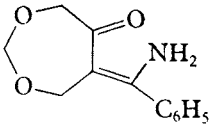
In the ^{13}C NMR spectrum the corresponding triplets for the carbon atoms $C_{(2)}$, $C_{(4)}$, and $C_{(8)}$, which support the structure *VIIIa* proposed, are found at 94·73, 74·07, and 64·19 ppm. The rearrangement derivative *VIIIa* is formed in the high yield of 87%. From the reaction mixture we could isolate a further substance with λ_{max} = 307 nm, *i.e.* with a bathochromic shift by 11 nm as compared with *VIIIa*, and with an aldehydic proton signal at 9·07 ppm. Most likely this substance is the *trans* isomer of *VIIIa*. Further irradiation of pure *cis* isomer *VIIIa* gave an equilibrium mixture of the two derivatives (9 : 1 in favour of the *cis* isomer).

The photolysis of substituted 8-(X-phenyl)-3,5,10-trioxa-9-azabicyclo[5,3,0]dec--8-enes (X = 4-F, 4-Cl, 3-CH_3, 4-OCH_3) showed an analogous course. The structure assignment to the rearrangement products formed, *i.e.* 6-(X-phenyl)-7-formyl--2,4,5,8-tetrahydro-1,3-dioxa-5-azocines *VIIIf* (86%), *VIIIg* (66%), *VIIIi* (47%), *VIIIj* (22%), was carried out as in the previous case. The yield of the 4-Cl derivative

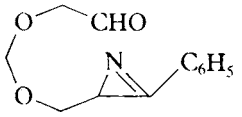
(66%) was achieved by carrying out the photochemical reaction in the presence of one equivalent of triethylamine. Without triethylamine the yield is much lower. The low yield of the methoxy derivative *VIIIj* was achieved at 40% conversion only, because otherwise the derivative *VIIIj* undergoes subsequent photochemical reactions. The yield is 55% with respect to the *IVj* amount reacted. The derivative *IVh* with bromo substituent at *para* position only gives polymeric products both in the presence and in the absence of triethylamine. Polymerization also proceeds with *IVl* and *IVm*. This finding agrees with literature data[16] about photosubstitution of halogens whose rate increases in the order F < Cl < Br and *o* > *m* > *p*. When following the photolysis of *VIIIh* by UV spectroscopy (conc. $5 \cdot 10^{-5}$ mol l^{-1}) without triethylamine, we only observed a decrease of the absorption maximum of the starting isoxazoline *IVh*, whereas the same reaction carried out with excess triethylamine was accompanied by appearing of the absorption maximum of the rearrangement product *VIIIh* which disappears in the further reaction course, the only products being polymeric materials again. The isoxazoline *IVk* with a nitro group in the aromatic ring is photostable at the same reaction conditions.



IX



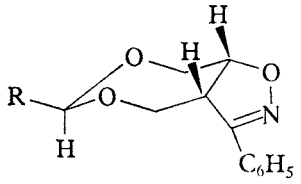
X



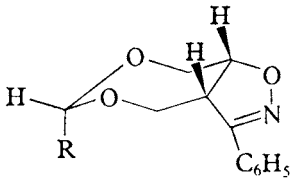
XI

The photolysis of the diastereoisomers of 4-phenylsubstituted *endo-IVb* and *exo-IVc* isoxazolines gives the identical product, 2,6-diphenyl-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIb*). Also the 4-methylsubstituted *endo-IVd* and *exo-IVc* isoxazolines give, on irradiation, the same product, 2-methyl-6-phenyl-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIId*). The structures *VIIIb* and *VIIId* were proved on the basis of analogy.

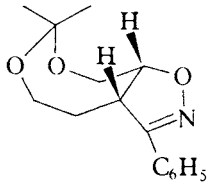
The derivatives of 2,4,5,8-tetrahydro-1,3-dioxa-5-azocine *VIII* and the derivatives of 2,3-dihydro-6*H*-1,3-oxazine *II* (refs[10,11]) are presumed to be formed by the same mechanism (Scheme 1). The homolysis of N—O bond in *IV* and rearrangement of *V* gives the diradical *VI* stabilized by resonance with *p*-electrons of the oxygen atom: recombination of *VI* produces 2,4,7,8-tetrahydro-1,3-dioxa-5-azocine *VII*.



IV endo



IV exo



XII

It is not quite clear whether the 1,3-sigmatropic shift *VII*→*VIII* proceeds thermally and photochemically or only photochemically. As the photochemical rearrangement results in the loss of the element of diastereoisomerism of the bicyclic system, both the *endo* and the *exo* diastereoisomers give the same rearrangement product.

When UV spectra were followed during the photolysis of the isoxazolines *IV* (at low concentration of $5 . 10^{-5}$ mol l^{-1}) using the radiation wavelength of 253·7 nm, isobestic points were found at 210, 247, and 276 nm, which indicates a photochemical reaction type A → B, the ED diagrams being linear, too. We also carried out quantitative measurements of the photorearrangement *IV* → *VIII*. The quantum yield Φ of the photorearrangement *IVa*→*VIIIa* of the parent non-substituted derivative is 0·025. In the photorearrangement *I*→*II* producing a six-membered heterocycle the quantum yield was $\Phi = 0{\cdot}08$ (refs[10,11]), which correlates with the finding that the quantum yield Φ is the greater the smaller is the ring[6,7]. The reaction *IV*→*VIII* proceeds in the same way whether or not oxygen is present, and we presume the singlet mechanism for it in accordance with refs[6–9].

Measurements of the quantum yields Φ for the 4-phenyl and 4-methyl substituted isoxazolines showed that the respective *exo* diastereoisomers exhibit higher values ($\Phi = 0{\cdot}025$ and 0·040 for *IVc* and *IVe*, respectively) than the corresponding *endo* isomers ($\Phi = 0{\cdot}009$ and 0·024 for *IVb* and *IVd*, respectively). As it has already been stated, the respective exo derivatives exhibit higher λ_{max} values of the longest-wave maximum and the presence of an additional absorption maximum at about 240 nm (as compared with the *endo* isomers). The higher rate of photorearrangement of *IVc*

(as compared with that of *IVb*) is seen in Fig. 1 giving the dependence of concentration (determined by HPLC) on the irradiation time for the reactions *IVc*→*VIIIb* and *IVb*→*VIIIb*. From the graph it is seen that the rearrangement product *VIIb* is decomposed on prolonged irradiation. The quantum yields were also measured for the X-phenylsubstituted derivatives: $\Phi = 0{\cdot}03$ and 0·011 for *IVf* and *IVg*, respectively.

On the basis of the results given and of our previous communications, the transformation *I*→*II* can be formulated as a new synthesis principle for preparation of heterocyclic compounds: the isoxazolines prepared from n-membered heterocycles and having a further oxygen atom at β position with respect to the isoxazoline oxygen atom can be submitted to a photorearrangement giving high yields of $(n + 1)$-membered heterocyclic compounds containing both oxygen and nitrogen atoms.

EXPERIMENTAL

The melting points were not corrected. The ^{1}H NMR spectra were measured with a Tesla BS 487 C apparatus in deuteriochloroform. The ^{13}C NMR spectra were measured with a JEOL apparatus using tetramethylsilane as the internal standard. The mass spectra were measured with a MS 902 S apparatus with direct inlet system, the ionization energy of 70 eV. The UV spectra were measured with a Perkin Elmer 323 spectrophotometer in thermostated cells in methanol. The ε values are given in $m^2\ mol^{-1}$.

The 2-substituted 1,3-dioxep-5-enes (*III*) were prepared by reaction of the respective aldehyde with *cis*-2-butene-1,4-diol with catalytic effect of *p*-toluenesulphonic acid[18], the benzene-

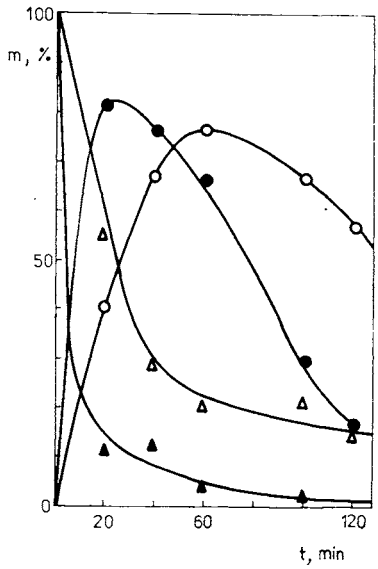


FIG. 1

Dependence of the product distribution from compounds *IVb* and *IVc* on the irradiation time. Symbols △ and ○ show amount of *IVb*→*VIIIb*, ▲ and ● *IVc*→*VIIIb*, respectively, in the photolysis in methanol

hydroximic acid chlorides were prepared by action of chlorine on the respective oximes in chloroform[19], the isoxazolines *IVi,j* were prepared by the method *B* (reaction of the respective oximes with sodium hypochlorite in the presence of triethylamine as the catalyst)[14]. The photochemical reactions were carried out with application of a low-pressure discharge lamp Toshiba GL-15 (15 W) in a quartz burner. The reaction was realized in a thermostated 300 ml reactor[20] with forced circulation of the irradiated solution at 25°C. The reaction course was followed by TLC (Silufol) and UV spectral measurements. Determination of the quantum yields of the reaction was described earlier[17].

Isoxazoline Derivatives

A) Solution of 13 mmol triethylamine in 20 ml ether was added to a solution of 10 mmol benzenehydroximic acid chloride and 10 mmol dipolarophile in 20 ml ether during 1 h with stirring and cooling at 0–5°C. The mixture was stirred at room temperature overnight, the separated triethylamine hydrochloride was removed by filtration, and the filtrate was evaporated in vacuum to give the respective isoxazoline which was purified by recrystallization or by column chromatography.

B) A solution of 21 mmol substituted benzaldoxime in 10 ml dichloromethane was added to a mixture of 21 mmol dipolarophile, 0·2 g (2 mmol) triethylamine, 20 ml 11% sodium hypochlorite solution (2·5 g NaClO, 34 mmol), and 15 ml dichloromethane at 0°C within 15 min. After 3 h stirring, the layers were separated, the aqueous layer was extracted with 3 × 20 ml dichloromethane, the combined organic portions were dried over magnesium sulphate and evaporated in vacuum. The product obtained was recrystallized.

8-*Phenyl*-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVa): Method *A*, from 1,3-dioxep-5-ene, yield 54%, m.p. 134–135°C. For $C_{12}H_{13}NO_3$ (219·2) calculated: 65·74% C, 5·98% H, 6·39% N; found: 65·66% C, 6·02% H, 6·28% N. UV spectrum: λ_{max} (log ε): 260 nm (2·97). Mass spectrum: *m/z* 219 M^+. ^{1}H NMR spectrum (C^2HCl_3): 7·25–7·71 (m, 5 H, aromatic H), 4·88 (d, J = 6·0 Hz, 1 H, 1-H), 4·63 (d, 1 H, 7-H), 3·82–4·87 (m, 6 H, 2-H, 4-H, 6-H). ^{13}C NMR spectrum (C^2H_3CN): 158·28 (s, $C_{(8)}$), 130·86, 130·47, 129·95, 127·93, 118·45 (aromatic C), 99·54 (t, $C_{(4)}$), 84·41 (d, $C_{(1)}$), 71·28 (t, $C_{(2)}$), 68·61 (t, $C_{(6)}$), 52·89 (d, $C_{(7)}$).

Reaction of benzenenitriloxide with 2-phenyl-1,3-dioxep-5-ene: Method *A*, the evaporation residue was separated by column chromatography (silica gel) with chloroform as eluent to give: *a*) The *endo* adduct 4,8-diphenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]-dec-8-ene (*IVb*), yield 52%, m.p. 174–176°C. For $C_{18}H_{17}NO_3$ (295·3) calculated: 73·20% C, 5·80% H, 4·74% N; found: 73·01% C, 5·97% H, 4·62% N. UV spectrum, λ_{max} (log ε): 260 nm (2·99). Mass spectrum: *m/z* 295 ($M^{\ddagger}$). ^{1}H NMR spectrum (C^2H_3CN): 7·25–7·77 (m, 10 H, aromatic H), 5·44 (s, 1 H, 4-H), 4·77–5·05 (m, 1 H, 1-H), 3·87–4·62 (m, 5 H, 2-H, 6-H, 7-H). ^{13}C NMR spectrum (C^2H_3CN): 158·40 (s, $C_{(8)}$), 140·30, 130·28, 129·88, 129·42, 127·93, 118·30 (aromatic C), 107·40 (d, $C_{(4)}$), 84·10 (d, $C_{(1)}$), 70·90 (t, $C_{(2)}$), 66·90 (t, $C_{(6)}$), 52·71 (d, $C_{(7)}$). b) The *exo*-adduct 4,8-diphenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-ene (*IVc*), yield 23%, m.p. 136–137°C. For $C_{18}H_{17}NO_3$ (295·3) calculated: 73·20% C, 5·80% H, 4·74% N; found: 73·44% C, 5·69% H, 5·03% N. UV spectrum, λ_{max} (log ε): 266 nm (3·03). Mass spectrum: *m/z* 295 ($M^{\ddagger}$). ^{1}H NMR spectrum (C^2H_3CN): 7·40–7·87 (m, 10 H, aromatic H), 5·71 (s, 1 H, 4-H), 4·70–4·90 (m, 1 H, 1-H), 3·68–4·47 (m, 5 H, 2-H, 6-H, 7-H). ^{13}C NMR spectrum (C^2H_3CN): 158·90 (s, $C_{(8)}$), 139·60, 131·24, 130·10, 129·62, 129·23, 127·93, 118·35 (aromatic C), 104·86 (d, $C_{(4)}$), 84·71 (d, $C_{(1)}$), 65·68 (t, $C_{(2)}$), 63·93 (t, $C_{(6)}$), 52·10 (d, $C_{(7)}$).

Reaction of benzenenitriloxide with 2-methyl-1,3-dioxep-5-ene: Method *A*, the evaporation residue was purified by column chromatography (silica gel, chloroform) to give: *a*) The *endo*

adduct 4-methyl-8-phenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-ene (*IVd*), yield 71%, m.p. 174–176°C. For $C_{13}H_{15}NO_3$ (233·3) calculated: 66·93% C, 6·48% H, 6·01% N; found: 67·14% C, 6·67% H, 5·92% N. UV spectrum, λ_{max} (log ε): 261 nm (3·00). Mass spectrum: *m/z* 233 (M^+). ^{1}H NMR spectrum (C^2HCl_3): 7·37–7·65 (m, 5 H, aromatic H), 4·61–4·89 (m, 2 H, 1-H, 4-H), 3·70–4·49 (m, 5 H, 2-H, 6-H, 7-H), 1·29 (d, J = 5·0 Hz, CH_3). ^{13}C NMR spectrum (C^2H_3CN): 158·50 (s, $C_{(8)}$), 130·66, 129·88, 127·93, 118·44 (aromatic C), 105·84 (d, $C_{(4)}$), 84·14 (d, $C_{(1)}$), 70·43 (t, $C_{(2)}$), 66·66 (t, $C_{(6)}$), 52·69 (d, $C_{(7)}$), 21·57 (q, CH_3). *b*) The *exo* adduct 4-methyl-8-phenyl-3,5,10-trioxa-9-azabicyclo[5,3,0]dec-8-ene (*IVe*), yield 10%, m.p. 113–115°C. For $C_{13}H_{15}$. $.NO_3$ (233·3) calculated: 66·93% C, 6·48% H, 6·01% N; found: 66·81% C, 6·47% H, 5·98% N. UV spectrum, λ_{max} (log ε): 265 nm (2·97), 244 nm (sh, 2·88). ^{1}H NMR spectrum (C^2HCl_3): 7·26–7·70 (m, 5 H, aromatic H), 4·85–5·10 (m, 1 H, 1-H), 4·87 (q, J = 5·1 Hz, 1 H, 4-H), 3·79–4·39 (m, 5 H, 2-H, 6-H, 7-H), 1·34 (d, 3 H, CH_3). ^{13}C NMR spectrum (C^2H_3CN): 158·67 (s, $C_{(8)}$), 133·65, 131·25, 130·01, 128·45, 127·93, 118·38 (aromatic C), 104·74, 104·74 (d, $C_{(4)}$), 84·53 (d, $C_{(1)}$), 66·21 (t, $C_{(2)}$), 64·71 (t, $C_{(6)}$), 52·50 (d, $C_{(7)}$), 20·66 (q, CH_3).

8-(4-*Fluorophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVf): Method A, from 1,3-dioxep-5-ene, yield 40%, m.p. 145–147°C. For $C_{12}H_{12}FNO_3$ (237·2) calculated: 60·76% C, 5·10% H, 5·90% N; found: 60·91% C, 5·21% H, 5·85% N. UV spectrum, λ_{max} (log ε): 258 nm (2·89). ^{1}H NMR spectrum (C^2HCl_3): 6·98–7·80 (m, 4 H, aromatic H), 3·79–5·02 (m, 8 H). ^{13}C NMR spectrum (C^2HCl_3): 156·46 (s, $C_{(8)}$), 172·18, 129·23, 124·94, 116·88 (aromatic C), 98·43 (t, $C_{(4)}$), 83·68 (d, $C_{(1)}$), 68·81 (t, $C_{(2)}$), 66·27 (t, $C_{(6)}$), 52·11 (d, $C_{(7)}$).

8-(4-*Chlorophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVg): Method A, from 1,3-dioxep-5-ene, yield 71%, m.p. 163–165 °C. For $C_{12}H_{12}ClNO_3$ (253·7) calculated: 56·82% C, 4·77 H, 5·52% N; found: 57·07% C, 5·00% H, 5·34% N. UV spectrum, λ_{max} (log ε): 264 nm (3·11). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 7·45–7·82 (m, 4 H, aromatic H), 4·80–5·05 (m, 1 H, 1-H), 3·79–4·57 (m, 6 H). ^{13}C NMR spectrum (C^2HCl_3): 156·46 (s, $C_{(8)}$), 136·18, 129·23, 128·19, 127·35 (aromatic C), 98·43 (t, $C_{(4)}$), 83·82 (d, $C_{(1)}$), 68·81 (t, $C_{(2)}$), 66·27 (t, $C_{(6)}$), 51·91 (d, $C_{(7)}$).

8-(4-*Bromophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVh): Method *A*, from 1,3-dioxep-5-ene, yield 70%, m.p. 184–188°C. For $C_{12}H_{12}BrNO_3$ (298·14) calculated: 48·34% C, 4·06% H, 4·70% N; found: 48·48% C, 4·11% H, 4·57% N. UV spectrum, λ_{max} (log ε): 265 nm (3·00). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 7·64 (s, 4 H, aromatic H), 4·75 to 4·95 (m, 1 H, 1-H), 3·75–4·50 (m, 6 H). ^{13}C NMR spectrum (C^2HCl_3): 156·59 (s, $C_{(8)}$), 132·16, 128·39, 127·74, 124·49 (aromatic C), 98·50 (t, $C_{(4)}$), 83·82 (d, $C_{(1)}$), 68·74 (t, $C_{(2)}$), 66·27 (t, $C_{(6)}$), 51·85 (d, $C_{(7)}$).

8-(4-*Methylphenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVi): Method *B*, from 1,3-dioxep-5-ene, yield 70%, m.p. 159–162°C. For $C_{13}H_{15}NO_3$ (233·3) calculated: 66·94% C, 6·48% H, 6·00% N; found: 67·02% C, 6·72% H, 5·95% N. UV spectrum, λ_{max} (log ε): 263 nm (3·04). ^{1}H NMR spectrum (C^2HCl_3): 7·12–7·67 (m, 4 H, aromatic H), 3·85–5·00 (m, 8 H), 2·37 (s, 3 H). ^{13}C NMR spectrum (C^2HCl_3): 157·37 (s, $C_{(8)}$), 140·47, 129·69, 126·89, 125·98 (aromatic C), 98·37 (t, $C_{(4)}$), 83·56 (d, $C_{(1)}$), 68·61 (t, $C_{(2)}$), 66·40 (t, $C_{(6)}$), 52·11 (d, $C_{(7)}$), 21·44 (q, 4-methyl-C).

8-(4-*Methoxyphenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVj): Method *B*, from 1,3-dioxep-5-ene, yield 68%, m.p. 141–144°C. For $C_{13}H_{15}NO_4$ (249·2) calculated: 62·65% C, 6·07% H, 5·62% N; found: 62·78% C, 6·28% H, 5·78% N. UV spectrum, λ_{max} (log ε): 269 nm (3·06). ^{1}H NMR spectrum (C^2HCl_3): 7·47–7·77 (m, 2 H, aromatic H), 6·82–7·10 (m, 2 H, aromatic H), 3·90–5·00 (m, 8 H), 3·82 (s, 3 H). ^{1}H NMR spectrum (C^2HCl_3): 156·98 (s, $C_{(8)}$), 161·13, 128·45, 121·24, 114·42 (aromatic C), 98·30 (t, $C_{(4)}$), 83·49 (dd, $C_{(1)}$), 68·55 (t, $C_{(2)}$), 66·40 (t, $C_{(6)}$), 55·36 (q, 4-methoxy-C), 52·17 (d, $C_{(7)}$).

8-(3-*Nitrophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVk): Method *A*, from 1,3-dioxep--5-ene, yield 74%, m.p. 145—147°C (acetone). For $C_{12}H_{12}N_2O_5$ (264·2) calculated: 54·54% C, 4·58% H, 10·60% N; found: 54·73% C, 4·34% H, 10·31% N. UV spectrum, λ_{max} (log ε): 257 nm (3·02) and 315 nm (2·20). ^{1}H NMR spectrum (hexadeuterioacetone): 7·67—8·51 (m, 4 H, aromatic H), 4·90 (d, 1 H, 1-H), 3·58—4·59 (m, 6 H). ^{13}C NMR spectrum (C^2HCl_3): 155·61 (s, $C_{(8)}$), 148·59, 132·81, 130·79, 130·14, 124·63, 121·63 (aromatic C), 98·63 (t, $C_{(4)}$), 84·27 (d, $C_{(1)}$), 69·33 (t, $C_{(2)}$), 66·34 (t, $C_{(6)}$), 51·72 (d, $C_{(7)}$).

8-(3-*Chlorophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVl): Method *A*, from 1,3-dioxep--5-ene, yield 61%, m.p. 123—124°C. For $C_{12}H_{12}ClNO_3$ (253·68) calculated: 56·82% C, 4·77% H, 5·52% N; found: 56·71% C, 4·84% H, 5·41% N. ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 7·47—7·73 (m, 4 H, aromatic H), 4·88 (d, 1 H, 1-H), 3·81—4·48 (m, 6 H).

8-(3-*Bromophenyl*)-3,5,10-*trioxa*-9-*azabicyclo*[5,3,0]*dec*-8-*ene* (IVm): Method *A*, from 1,3--dioxep-5-ene, yield 74%, m.p. 171—173°C (acetone). For $C_{12}H_{12}BrNO_3$ (298·14) calculated: 48·34% C, 4·06% H, 4·70% N; found: 48·51% C, 4·31% H, 4·92% N. ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 7·51—7·86 (m, 4 H, aromatic H), 4·87 (d, 1-H), 3·83—4·46 (m, 7 H). ^{13}C NMR spectrum (C^2HCl_3): 155·84 (s, $C_{(8)}$), 133·04, 130·46, 129·76, 125·43 (aromatic C), 98·52 (t, $C_{(4)}$), 83·89 (d, $C_{(1)}$), 68·80 (t, $C_{(2)}$), 66·23 (t, $C_{(6)}$), 51·83 (d, $C_{(7)}$).

Photochemical Rearrangement of Compounds *IV*

IVa: A solution of 0·5 g (2·28 mmol) *IVa* in 270 ml acetonitrile was irradiated 5 h, concentrated in vacuum, and triturated with 10 ml dry ether to give 0·35 g (70%; 87% with respect to reacted *IVa*) 6-phenyl-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIa*), m.p. 168—171°C. For $C_{12}H_{13}NO_3$ (219·2) calculated: 65·74% C, 5·98% H, 6·39% N; found: 65·73% C, 6·15% H, 6·08% N. UV spectrum, λ_{max} (log ε): 296 nm (3·16). Mass spectrum, *m/z* 219 ($M^{+\cdot}$). ^{1}H NMR spectrum (C^2HCl_3): 8·89 (s, 1 H, CHO), 7·40 (s, 5 H, aromatic H), 5·55 (m, 1 H, 5-H), 4·91 (s, 1 H, 2-H), 4·79 (s, 5 H, 2-H, 4-H, 8-H). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·54 (d, CHO), 162·82 (s, $C_{(7)}$), 136·44, 129·81, 128·25 (aromatic C), 110·71 (s, $C_{(6)}$), 94·73 (t, $C_{(2)}$), 74·07 (t, $C_{(4)}$), 64·19 (t, $C_{(8)}$). Preparative TLC (silica gel, cyclohexane–ethyl acetate 1 : 2) of the filtrate gave 0·09 g (20%) unreacted *IVa* and 30 mg (probably) *trans*-isomer *VIIIa* (UV spectrum, λ_{max} 307 nm; ^{1}H NMR spectrum (C^2HCl_3): 9·07 (s, 1 H, CHO), 7·45 (s, 5 H, aromatic H), 4·82 (s, 4 H, 2-H, 4-H), 4·62 (s, 2 H, 8-H)).

IVb: Analogous reaction to that used for *IVa* gave 2,6-diphenyl-7-formyl-2,4,5,8-tetrahydro--1,3-dioxa-5-azocine (*VIIIb*), yield 77%, m.p. 196—198°C. For $C_{18}H_{17}NO_3$ (295·3) calculated: 73·20% C, 5·80% H, 4·74% N; found: 73·59% C, 6·09% H, 5·00% N. UV spectrum, λ_{max} (log ε): 299 nm (3·16). Mass spectrum: *m/z* 295 ($M^{+\cdot}$). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 8·67 (s, 1 H, CHO), 7·20—7·51 (m, 10 H, aromatic H), 5·55 (s, 1 H, 2-H), 5·16 (d, J = = 15 Hz, 1 H, 4-H_B), 4·44 (d, 1 H, 4-H_A), 4·29—5·10 (m, 2 H, 8-H). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·42 (d, CHO), 163·01 (s, $C_{(7)}$), 139·10, 136·20, 129·88, 128·19, 127·80, 126·17 (aromatic C), 110·90 (s, $C_{(6)}$), 102·85 (d, $C_{(2)}$), 73·29 (t, $C_{(4)}$), 63·86 (t, $C_{(8)}$).

IVc: The irradiation of *IVc* under the same conditions gave *VIIIb*.

IVd: Analogous reaction to that used for *IVa* gave 2-methyl-6-phenyl-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIId*), yield 69%, m.p. 198—202°C. For $C_{13}H_{15}NO_3$ (233·3) calculated: 66·93% C, 6·48% H, 6·01% N; found: 67·12% C, 6·18% H, 5·88% N. UV spectrum, λ_{max} (log ε): 297 nm (3·15). Mass spectrum, *m/z* 233 ($M^{+\cdot}$). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 8·62 (s, 1 H, CHO), 7·20—7·50 (m, 5 H, aromatic H), 5·11 (d, J = 15 Hz,

1 H, 4-H_A), 4·81 (s, 3 H, 5-H, 8-H), 4·68 (q, J = 4 Hz, 1 H, 2-H), 4·17 (d, 1 H, 4-H_B), 1·21 (d, 3 H, CH_3). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·35 (d, CHO), 162·89 (s, $C_{(7)}$), 136·31, 129·82, 128·13 (aromatic C), 110·78 (s, $C_{(6)}$), 101·23 (d, $C_{(2)}$), 73·03 (t, $C_{(4)}$), 63·22 (t, $C_{(8)}$), 21·12 (q, CH_3).

IVe: The irradiation of *IVe* under the same conditions gave *VIIId*.

IVf: A solution of 0·25 g (1·05 mmol) *IVf* in 300 ml acetonitrile was irradiated for 135 min and evaporated in vacuum; the residue was recrystallized from a mixture of dichloromethane and hexane to give 0·215 g (86%) 6-(4-fluorophenyl)-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa--5-azocine (*VIIIf*), m.p. 136—140°C. For $C_{12}H_{12}FNO_3$ (237·2) calculated: 60·76% C, 5·10% H, 5·90% N; found: 60·75% C, 5·13% H, 5·93% N. UV spectrum, λ_{max} (log ε): 235 nm (2·82), 296 nm (3·04). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 8·70 (s, 1 H, CHO), 7·37—7·50 (m, 4 H, aromatic H), 4·60—4·95 (m, 6 H). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·29 (d, CHO), 161·65 (s, $C_{(7)}$), 132·48, 131·90, 115·91, 114·48 (aromatic C), 111·04 (s, $C_{(6)}$), 94·79 (t, $C_{(2)}$), 74·00 (t, $C_{(4)}$), 64·39 (t, $C_{(8)}$).

IVg: A solution of 0·3 g (1·18 mmol) *IVg* in 300 ml acetonitrile with addition of 1 equivalent of triethylamine was irradiated for 150 min and evaporated in vacuum; the residue was recrystallized from a dichloromethane-hexane mixture to give 0·20 g (66%) 6-(4-chlorophenyl)-7-formyl--2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIg*), m.p. 132—135°C. For $C_{12}H_{12}ClNO_3$ (253·7) calculated: 56·82% C, 4·77% H, 5·52% N; found: 56·83% C, 4·91% H, 5·34% N. UV spectrum, λ_{max} (log ε): 240 nm (3·02), 296 nm (3·08). ^{1}H NMR spectrum (hexadeuteriodimethyl sulphoxide): 8·72 (s, 1 H, CHO), 8·07 (broad band, 1 H, NH), 7·30—7·65 (m, 4 H, aromatic H), 4·65—4·95 (m, 6 H). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·16 (d, CHO), 161·39 (s, $C_{(7)}$), 135·15, 134·56, 131·70, 128·26 (aromatic C), 110·97 (s, $C_{(6)}$), 94·73 (t, $C_{(2)}$), 74·00 (t, $C_{(4)}$), 64·19 (t, $C_{(8)}$).

IVi: A solution of 0·3 g (1·28 mmol) *IVi* in 300 ml acetonitrile was irradiated for 150 min and evaporated in vacuum; the residue was recrystallized from a dichloromethane–hexane mixture to give 0·14 g (47%) 6-(4-methylphenyl)-7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIi*), m.p. 163—166°C. For $C_{13}H_{15}NO_3$ (233·3) calculated: 66·94% C, 6·48% H, 6·00% N; found: 66·77% C, 6·69% H, 5·95% N. UV spectrum, λ_{max} (log ε): 240 nm (3·08), 298 nm (3·20). ^{1}H NMR spectrum (C^2HCl_3): 8·91 (s, 1 H, CHO), 7·10—7·40 (m, 4 H, aromatic H), 4·72—4·97 (m, 6 H), 2·39 (s, 3 H, CH_3). ^{13}C NMR spectrum (hexadeuteriodimethyl sulphoxide): 188·42 (d, CHO), 162·75 (s, $C_{(7)}$), 139·56, 133·51, 129·81, 128·71 (aromatic C), 110·71 (s, $C_{(6)}$), 94·79 (t, $C_{(2)}$), 74·00 (t, $C_{(4)}$), 64·51 (t, $C_{(8)}$), 20·79 (q, CH_3).

IVj: A mixture of 0·3 g (1·20 mmol) *IVj* and 300 ml cyclohexane was irradiated for 120 min and concentrated in vacuum. The residue was submitted to column chromatography (silica gel, chloroform) to give 180 mg (60%) starting compound and 65 mg (22%) 6-(4-methoxyphenyl)--7-formyl-2,4,5,8-tetrahydro-1,3-dioxa-5-azocine (*VIIIj*), m.p. 148—150°C. For $C_{13}H_{15}NO_4$ (249·2) calculated: 62·65% C, 6·07% H, 5·62% N; found: 62·41% C, 6·27% H, 5·52% N. UV spectrum, λ_{max} (log ε): 245 nm (2·79), 300 nm (3·00). ^{1}H NMR spectrum (C^2HCl_3): 8·87 (s, 1 H, CHO), 6·82—7·42 (m, 4 H, aromatic H), 5·75 (broad band, 1 H, NH), 4·52—4·97 (m, 6 H), 3·85 (s, 3 H, OCH_3). ^{13}C NMR spectrum (C^2HCl_3): 190·50 (d, CHO), 162·17 (s, $C_{(7)}$), 161·52, 131·70, 128·39, 113·90 (aromatic C), 112·86 (s, $C_{(6)}$), 96·74 (t, $C_{(2)}$), 74·46 (t, $C_{(4)}$), 67·44(t,$C_{(8)}$), 55·36 (q, OCH_3).

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