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The photoreactivity of 3-methyl-4-nitro-5-styrylisoxazole in solution and adsorbed on silica gel was studied and the photodimers obtained were identified. The structures of the photoproducts were assigned on the basis of mass and nmr spectra and chemical behavior. Irradiation of the title compound adsorbed on solid or slurry silica gel leads to the same photoproducts obtained from the solution but with a different yield.

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The photoreactivity of styryl derivatives have been studied either in solution (1-7) or in the solid state (2b,3,6,8-10). In many cases the photoreactivity correlated to the molecular structure, is also dependent on the irradiation phase. As an example, *trans*-cinnamic acid photodimerizes in the solid state but not in solution (11), whereas *trans*-stilbene photoreacts only in solution to give two photodimers, *cis*-stilbene (6) and dihydrophenanthrene (12).

The photoreactivity in the solid state of these type of compounds have been rationalized on the basis of the topochemical postulate (6,9) or alternatively stacking faults were invoked for non-topochemical products (6). Many aspects of the photobehavior in solution of a large number of stilbene (1b), 2-styrylpyridines (2a,b), calchone (3), styrene (4) and *trans*-4-styrylbenzo[*h*]quinoline (5) were investigated.

Recently, during a study on the photoreactivity of styrylthiophenes, attention to a correlation between the monomer crystal structures and their solution photodimerization was proposed on the basis of non-bonding attractive interaction (6).

As an example of the photochemistry of styryl and isoxazole derivatives, we refer to the photochemical behavior of 3-methyl-4-nitro-5-styrylisoxazole (1) in benzene solution and adsorbed on silica gel in comparison with that of 1 in the solid state. The photoproduct obtained by the action of sunlight on 1 in the solid state was shown to be a dimer (13). The photoreactivity of 1 in the solid state was reinvestigated and the structure of

the dimer established as an α -truxillic type on the basis of chemical behavior, nmr and Mass spectra (10).

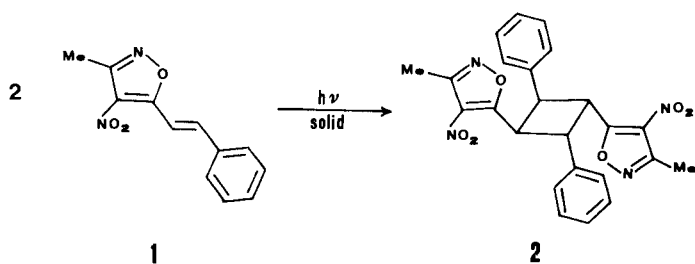
Results and Discussion.

The molecular structure of 1 suggests several photochemical reactions in solution, namely: (i) isoxazole \rightarrow oxazole isomerization; (ii) *trans* \rightarrow *cis* isomerization; (iii) (2+2) dimerization on the exocyclic double bond, leading to four isomers for which cyclobutane type structures are expected.

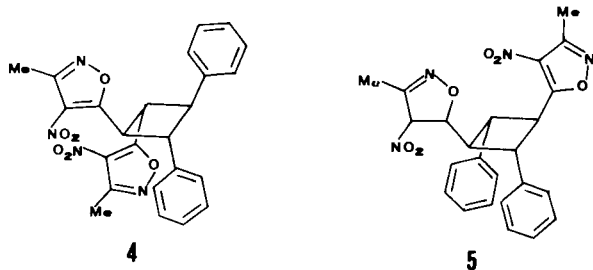
In order to test the photoreactivity of 1 in solution it was found convenient to irradiate benzene solutions of 3-methyl-4-nitro-5-styrylisoxazole using the filtered light of a medium pressure mercury lamp.

The tlc (benzene as eluent) of the irradiated solution shows the presence of six spots and material with $R_f = 0$. By comparison of the R_f and others chemical and physical properties, 1 (unreacted monomer) and 2 (the centrosymmetric dimer obtained also from the solid state) were recognized.

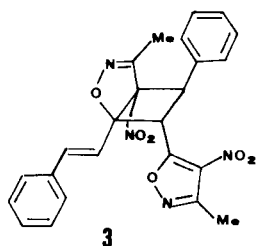
Chemical and spectroscopic methods were used to prove the structures of the others products. Three of them were identified as dimers and the molecular structures clarified. Column chromatography on silica gel (benzene as eluent) of the irradiated solution separated six products in the following order: 1, 3, 2, 4, 5, and 6. The mass spectra of compounds 3, 2, 4 and 5 show parent peaks at m/e 460 in agreement with dimers of 1, and peaks at 230 (monomer ion, $M/2$). In addition, 4 shows a peak at m/e 180 for $(C_6H_5-CH=CH-C_6H_5)^+$ suggesting a truxinic type structure for this dimer. The nmr spectra of 2, 4, and 5 show symmetrical AA'BB' multiplets, typical for hydrogens of cyclobutane systems, centered at δ 5.20 (2), δ 4.55 (4) and δ 4.65 (5); methyl singlets at δ 2.33 (2) and δ 2.51 (4,5), and phenyl signals at δ 7.22 (2), δ 7.32 (4) and δ 7.30 (5). Following the suggestion of Ben-Efraim and Green (14), 4 and 5 showing the same mid-point of cyclobutane hydrogens multiplets, should have the same carbon atoms skeleton, but different from



that of **2**. On the basis of the attribution to **2** of the α -truxillic type structure (10) and considering mass spectra results, compounds **4** and **5** should have the following δ -truxinic and ϵ -truxillic type structures, respectively.



Compound **3** shows two phenyl signals at δ 7.28 and δ 7.40, two methyl singlets (δ 1.49 and δ 2.50) and two AX systems (δ_A 7.02, δ_X 6.11, $J_{AX} = 16$ Hz), (δ_A 5.02, δ_X 5.53, $J_{AX} = 12$ Hz). The nmr signals for phenyl at δ 7.28 and methyl at δ 2.50 together with the presence of a peak at m/e 230 ($M/2$) in the mass spectrum strongly suggest that the structure of **3** should contain a system with saturated bond of the original styryl moiety. In addition, the nmr spectrum of **3** shows signals in agreement with *trans*-hydrogens of a double bond. The above data strongly suggest the following structure for **3**.



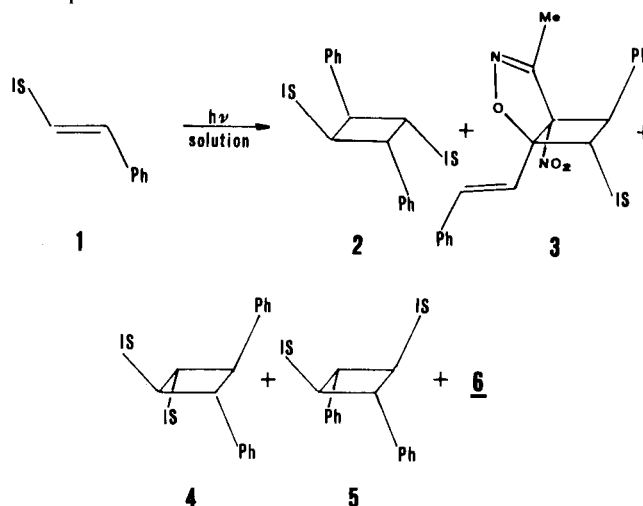
Among the four isomers consistent with a cycloaddition of the styryl double bond on the 4,5-isoxazole positions, the structure proposed accounts for the low δ value of the 3-methyl of the isoxazoline system compared with those reported (δ 1.9-2.1) (15). The shift should be caused by a shielding-effect due to the phenyl ring facing the methyl group, only in the structure reported for **3**. This structure was finally elucidated by X-ray analysis (16) whereas the above structures for **2**, **4** and **5** were confirmed through the J constant values (Table I) calculated by computer simulation for AA'BB' spectra following the literature (17).

Table I

Compound	J_{AB}	$J_{AB'}$	$J_{AA'}$	$J_{BB'}$
2	10.5	7.7	0.0	0.0
5	10.1	10.1	0.0	0.0
4	10.1	0.0	9.8	9.8

In addition, the alkaline hydrolysis of the isoxazole rings in the dimers **2**, **4** and **5** followed by acidification leads to the corresponding diphenylcyclobutane dicarboxilic acids which were recognized as α -truxillic, δ -truxinic and ϵ -truxillic acids, respectively.

The photoreactivity of **1** in benzene solution is summarized in the following scheme. The structure of compound **6** was not elucidated.



It appears interesting to draw attention to the fact that among the four dimers resulting from (2 + 2) styryl dimerization, only three were isolated and identified, the fourth dimer being the unexpected **3**. The β -truxinic type dimer or the *cis*-monomer were not detected in our case whereas they are reported in the photoreaction of other styryl derivatives. Additional work is necessary to clarify the determining factors for the outcome of photochemical reaction of **1** in solution.

Recently, the photoreactivity of adsorbed molecules on silica gel and other supports was reported (18a,b,c,19). In some cases the adsorption induces changes in the absorption

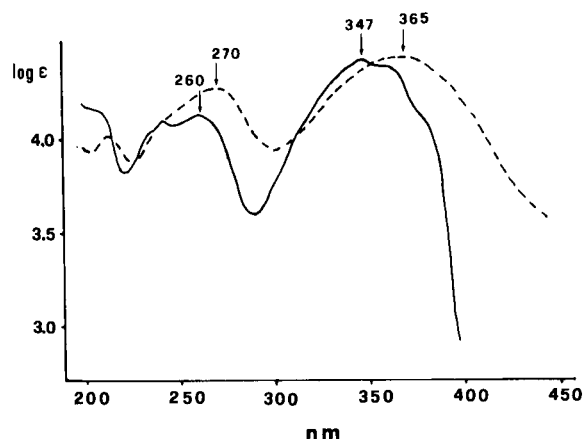


Figure 1) UV Spectra of 3-Methyl-4-nitro-5-styrylisoxazole in Cyclohexane (full line) and in Silica Gel Cyclohexane Slurry (dotted line).

Table 2
Relative Yields of Dimers of **1** Obtained under Different Experimental Conditions

Experimental Irradiation Phase	Relative Yields (%)				Unreacted Monomer (%)
	2	3	4	5	
Solid state	99	trace	-	trace	10
Benzene solution	35.7	4.5	44	15.7	42
Silica gel cyclohexane slurry	83.5	1.0	6.7	8.6	39
Solid silica gel	89	0.5	3.6	6.5	15

spectra and in the photoreactivity (18c).

Following this line, the uv spectrum of **1** taken in a suspension of a silica gel cyclohexane slurry compared with that in cyclohexane (Figure 1) shows a red-shift suggesting a strong interaction between compound **1** and silica gel. The photobehavior of **1** was investigated also when adsorbed on a silica gel cyclohexane slurry and on solid silica gel under the conditions reported in the experimental section. The dimers **2**, **3**, **4** and **5** were obtained by these two procedures in different ratios in comparison with the solution reaction as reported in Table 2.

It is noteworthy to consider the photoreactivity of **1** on solid silica gel which give rise to the photoproducts obtained also from benzene solution with less irradiation time in the first case. Irradiation of solid **1** with the glass filtered light of a 250 W mercury lamp confirmed, within experimental error, previous results (10); the use of HPLC allows the detection of small amounts of **3** and **5** (<1%).

The above findings together with those already reported (18a,b,c,19) stimulate the study of the photoreactions in dispersed solid surface which could give rise to different photobehavior from that observed in solution or in the solid state. In addition, examples of compounds photo-reacting when adsorbed on silica gel but not in the solid state are under study (20).

EXPERIMENTAL

Melting points are uncorrected. Uv spectra were determined on a Cary 14 spectrophotometer. Nmr spectra were recorded on a Perkin-Elmer R 32 using deuteriochloroform as solvent and reported in δ units with tetramethylsilane (TMS) as internal standard. Ir spectra were registered on a Perkin-Elmer Infracord 457 in potassium bromide pellets. Mass spectral data were taken with an Atlas CH-4 mass spectrometer. The samples were introduced *via* the direct inlet system. High Pressure Liquid Chromatography (HPLC) was performed using Waters model ALC/GPC-201 equipped with a prepacked μ -Porasil (4 mm x 30 cm) column and benzene/cyclohexane (40/60) as eluent. Detection and quantitative estimation of the products were obtained by the uv detector Perkin-Elmer model LC 55. Benzene solutions were irradiated in pyrex flasks with the light (filtered with copper sulfate saturated solution) of a medium pressure mercury lamp (250 W) at a distance of 30 cm. Separations of photoproducts from irradiated mixture were obtained by using column chromatography (120 cm length, 3 cm diameter) filled with silica gel G

type 60 (Merck) and benzene as eluent. Thin layer chromatographic plates [silica gel 60 F₂₅₄, layer thickness 0.25 mm (Merck)] were used for routine analyses (benzene as eluent) and mineral light lamp (Model UV SL-58) for revealing spots.

Irradiation of 3-Methyl-4-nitro-5-styrylisoxazole in Benzene Solution.

A benzene solution (50 ml.) of **1** (1.451 g.) was irradiated for one month. Tlc analysis showed the presence of six spots. A brownish portion with $R_f = 0$ was also present. Two spots were identified as due to **1** and **2** respectively, by comparison with authentic products. The irradiated solution was evaporated and the solid obtained was column chromatographed to give seven fractions which contained compounds **1** (370 mg.), **3** (37 mg.), **2**, **2** and **4**, **5** (221 mg.) and **6** (28 mg.), respectively. Fraction four rechromatographed in the same conditions separated **2** and **4**. The total amount of **2** and **4** was 369 mg. and 428 mg., respectively. The first and third fraction evaporated and crystallized from ethanol were recognized as **1** and **2**, respectively, by comparison with authentic samples (13,10).

Compound 3.

This compound, obtained from fraction **2**, was crystallized from ethanol, m.p. 189-190° dec.; uv: λ max (methanol): 253 nm ($\log \epsilon = 4.19$) nmr: δ 7.28 (S, 5H, aromatic), 7.40 (S, 5H, aromatic), 7.12-6.0 (AX, 2H, double bond), 5.6-4.95 (AX, 2H, cyclobutane), 2.5 (S, 3H, methyl), 1.48 (S, 3H, methyl); ms: m/e (relative intensity) 460 (0.007, molecular ion), 430 (0.03, M⁺-NO), 414 (0.62, M⁺-NO₂), 230 (100, M/2), 184 (12, M/2-NO₂); ir: 1610 cm⁻¹ (isoxazole ring), 1525, 1355 (NO₂ group), 980 (*trans* double bond).

Anal. Calcd. for C₂₄H₂₀N₄O₆: C, 62.61; H, 4.38; N, 12.17. Found: C, 62.69; H, 4.57; N, 12.37.

Compound 4.

This compound was crystallized from ethanol, m.p. 193-194°; uv: λ max (methanol) 265 nm ($\log \epsilon = 4.04$); nmr: δ 7.32 (S, 10, aromatic), 4.90-4.22 (AA'BB', 4H, cyclobutane), 2.51 (S, 6H, methyl); ms: m/e (relative intensity) 460 (0.002, molecular ion), 230 (31, M/2-NO₂), 180 (100, C₆H₅CH=CHC₆H₅⁺); ir: 1605 cm⁻¹ (isoxazole ring), 1522, 1365 (NO₂ group).

Anal. Calcd. for C₂₄H₂₀N₄O₆: C, 62.61; H, 4.38; N, 12.17. Found: C, 62.47; H, 4.48; N, 12.38.

Compound 5.

Evaporation of the fifth fraction gave **5** which was crystallized from ethanol, m.p. 224-225°; uv: λ sh (methanol) 260 nm ($\log \epsilon = 3.94$); nmr: δ 7.30 (S, 10H, aromatic), 5.02-4.25 (A₂B₂, 4H, cyclobutane), 2.51 (S, 6H, methyl); ms: m/e (relative intensity) 460 (0.02, molecular ion), 230 (100, M/2), 184 (29, M/2-NO₂); ir: 1605 cm⁻¹ (isoxazole ring), 1520, 1365 (NO₂ group).

Anal. Calcd. for C₂₄H₂₀N₄O₆: C, 62.61; H, 4.38; N, 12.17. Found: C, 62.56; H, 4.27; N, 11.88.

Compound 6.

Fraction 6 separated, after evaporation, a yellow solid which was tentatively crystallized from ethanol (needles). However, the small quantity available did not allow to characterize the above compound owing to the low purity reached.

Solid State Irradiation of 1.

Large scale preparation of 2 was performed by irradiation of 1 in the solid state, in Petri dishes and occasionally removed. Alternatively, 1 was deposited between two glass plates (≈ 0.3 mg./cm²) by evaporation of benzene saturated solution. In this case the yield of conversion of 1 to 2 was found to be 90% for 90 minutes of irradiation from each side. In addition, careful analysis of the photoproducts by HPLC showed the presence of small amount of 3 and 5 (< 1%). For these experiments, the light of a 250 W mercury lamp was used.

Irradiation of 1 Adsorbed on Solid Silica Gel or in a Silica Gel Cyclohexane Slurry.

In order to find the best ratio between 1 and silica, cyclohexane solution of 1 (44.7 mg./100 ml.) were added with increasing amount of silica gel (60 HR Merck). After agitation, the slurries were centrifuged and the supernatant analysed by uv absorption to test the concentration of 1 in solution. By this procedure it was observed that the added silica turned yellow as a result of adsorption of 1 from the uncoloured cyclohexane solution. When the ratio between silica gel/1 was 40/1 (w/w), the amount of 1 adsorbed was 98%. A cyclohexane solution (30 ml.) of 1 added with silica gel (1.022 g. previously heated at 200° for 2 hours and left to cool in a desiccator overnight) was agitated and the slurry centrifuged. The supernatant was separated and the slurry left to evaporate in Petri dishes overnight in the dark. The solid silica was then exposed to filtered light (copper sulfate aqueous solution) of a mercury lamp (250 W) for 30 hours. The slurry extracted in a Soxhlet extractor with acetone and evaporated gave a solid which solubilized in benzene was analysed using HPLC.

A system of two cylindrical pyrex coaxial cells (double walled) was used for the slurry irradiation. The lamp (Philips HPK 125 W) was placed axially and water was allowed to circulate in the inner cell to prevent heating of the outer container where the slurry, prepared as above was placed.

Alkaline Hydrolysis of 2.

Compound 2 (481 mg.) was refluxed under stirring with 30 ml. of sodium hydroxide (10%) for 9 hours. After cooling, the solid present (starting material, 62 mg.) was filtered off. The solution added with hydrochloric acid (1:1) gave α -truxillic acid (244 mg., m.p. 274° alcohol), identical with an authentic sample (11).

Alkaline Hydrolysis of 5.

Compound 5 (326 mg.) was refluxed under stirring with 40 ml. of sodium hydroxide (10%) for 8 hours. After cooling, the solid present (starting material, 51 mg.) was filtered off. The solution added with hydrochloric acid (1:1) precipitated ϵ -truxillic acid (66 mg.). Concentration of the aqueous solution separated additional solid (60 mg.) which added to the previous solid and crystallized (acetone-water) gave colourless needles, m.p. 189°, lit. 189°, 190-190.5°.

Alkaline Hydrolysis of 4.

Compound 4 (172 mg.) was refluxed under stirring with 30 ml. of sodium hydroxide (10%) for 4 hours. After cooling, the solid present (starting material 3 mg.) was filtered off. The solution added with hydrochloric acid (1:1) and left overnight gave

a precipitate (108 mg.) recognized as δ -truxinic acid, m.p. 174°, alcohol, lit. 174°.

Alkaline Hydrolysis of 3-Methyl-4-nitro-5-styrylisoxazole.

Compound 1 (473 mg.), added with 100 ml. of sodium hydroxide (10%), was refluxed for 7 hours. After cooling, the unreacted solid (221 mg.) was filtered off and the solution, acidified with hydrochloric acid (1:1) gave *trans*-cinnamic acid, (m.p. 133-134°, alcohol-water, identical with an authentic sample.

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