

STEREOCHEMISTRY AND PHOTOISOMERISATION
OF FURFURYLIDENE OXINDOLES*

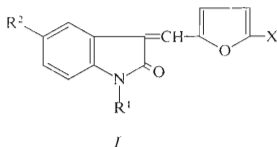
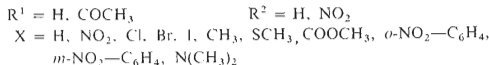
J.ŠTETINOVÁ, J.KOVÁČ, †J.SURÁ and M.DANDÁROVÁ

Department of Organic Chemistry,
Slovak Institute of Technology, 880 37 Bratislava

Received July 27th, 1976

Geometric isomers of furfurylideneoxindoles undergo photoisomerisation which was followed by UV and ¹H-NMR spectroscopy. The population of the isomers was determined semiquantitatively by thin-layer chromatography.

Synthesis of some furfurylideneoxindoles has been the subject of several papers¹⁻⁵, however, the stereochemistry of these compounds was not investigated. We reported⁶ the synthesis and physico-chemical properties of 3-(5-X-2-furfurylidene)oxindoles and their 5-nitro or 1-acetyl derivatives of the general formula *I*.



Thanks to the exocyclic double bond the compounds of the structure *I* can exist in two geometric isomers. In this paper the stereochemistry of furfurylideneoxindoles is studied, together with the photoisomerisation which we observed for these compounds.

The furfurylideneoxindoles *I* were prepared by condensation of oxindole, 5-nitro-oxindole and 1-acetyloxindole with 5-X-2-furancarbaldehydes, where X = H, NO₂, Cl, Br, I, CH₃, SCH₃, COOCH₃, *o*-NO₂-C₆H₄, *m*-NO₂-C₆H₄ and N(CH₃)₂.

* Part CIV in the series Furan Derivatives; Part CIII: Chem. Zvesti, in press.

and also by acetylation of the corresponding furfurylideneoxindoles^{1,2,6}. Thin-layer chromatography of the reaction product revealed the presence of two unequally populated geometric isomers. All the usual methods of separation of isomers proved to be unsuccessful in this case. Only later we have found that substituted furfurylideneoxindoles are photosensible and are isomerised by action of light on their solutions.

The geometric isomers of the parent compound of this type, 3-(2-furfurylidene)oxindole (*I*, $R^1 = R^2 = X = H$), were separated by preparative thin-layer chromatography on silica gel. In order to exclude photoisomerisation all the operations were carried out in the dark or in a dim red light. The thus obtained geometric isomers were identified by ¹H-NMR spectroscopy (Table I). The character and shape of the signals as well as the number of protons were in accord with the assumption of two geometric isomers *E* and *Z* which can exist in various conformers thanks to various orientations of the furan ring (Fig. 1). As seen from Table I, the ¹H-NMR spectra of the studied compounds differ most markedly in the H₄ signals of the indole part (*E*: 8.45 ppm; *Z*: 7.44 ppm) and in the H₁₀ signals of the furan part of the molecule (*E*: 6.91 ppm, *Z*: 8.32 ppm). The significantly smaller shielding of H₄ in the *E* isomer as compared with the *Z* isomer can be explained by the proximity of this proton

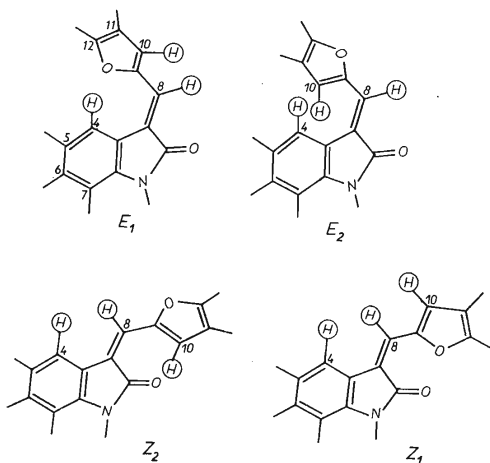


FIG. 1

Conformers of (*E*)- and (*Z*)-3-(2-Furfurylidene)oxindoles (*I*, $R^1 = R^2 = X = H$)

and the furan ring in the conformation E_1 in which the furan oxygen is in the immediate vicinity to H_4 . The arrangement E_1 is advantageous also sterically. The downfield shift of the H_{10} signal in the Z isomer is caused by the anisotropic effect of the carbonyl group in the conformation Z_2 . In the conformation Z_1 both of the oxygens would be very close to each other. Contrary to the case of benzylideneoxindoles^{7,8} where the configuration was assigned to the geometric isomers on the basis of chemical shifts of the olefinic proton, the isomers of furfurylideneoxindoles cannot be identified on the basis of the H_8 signals. The differences here are too small ($\Delta\sigma = 0.03$ ppm) because in the conformers E_1 and Z_2 the chemical shift of H_8 signals is compensated by both the oxygen atoms. In the E_1 form the carbonyl group is *cis* and the furan oxygen *trans* relative to H_8 ; in the Z_2 conformer the situation is reversed. Analogously to benzylideneoxindole and most of its derivatives⁷⁻¹⁰ also the obtained furfurylideneoxindole is predominantly the E -isomer which was assigned the conformation E_1 on the basis of the mentioned analysis. The minor reaction product is the second isomer which has the conformation Z_2 . In both cases a coplanar arrangement is impossible for steric reasons, as seen also by inspection of Stuart-Briegleb models of these compounds.

The photoisomerisation of furfurylideneoxindoles was followed by UV and $^1\text{H-NMR}$ spectroscopy and the ratio of isomers was determined by semiquantitative thin-layer chromatography. We measured the electronic absorption spectra in the region 300–500 nm, and investigated the spectral changes caused by action of light on the solutions of the studied compounds in solvents of low polarity (250 W projection lamp or by a UV source). Figs 2 and 3 depict the course of the photoisomerisation of (E)- and (Z)-isomers of 3(2-furfurylidene)oxindole (I , $R^1 = R^2 = X = \text{H}$) in toluene. After certain time of exposure to light an equilibrium was achieved (an almost identical spectrum was obtained starting from both isomers).

TABLE I

$^1\text{H-NMR}$ Data (δ , ppm; J , Hz) for (E)- and (Z)-3-(2-Furfurylidene)oxindoles (I , $R^1 = R^2 = X = \text{H}$)

| Isomer | H_{11} dd | H_7 bd | H_{10} d | H_6 dt | H_5 dt | H_8 s | H_{12} dd | H_4 bd | NH bs |
|--------|----------------|-------------|---------------|-------------|-------------|------------|----------------|-------------|----------|
| E^a | 6.61 | 6.90 | 6.91 | 7.03 | 7.25 | 7.45 | 7.76 | 8.45 | 8.56 |
| Z^a | 6.59 | 6.82 | 8.32 | 7.01 | 7.22 | 7.42 | 7.58 | 7.44 | 8.22 |

$^a J_{11,12} = 1.8$; $J_{10,11} = 3.5$; $J_{6,7} = 7.5$; $J_{5,7} = 1.5$; $J_{4,7} < 1$; $J_{10,12} < 1$; $J_{5,6} = 7.5$; $J_{4,6} = 1.5$; $J_{4,5} = 7.5$.

Photoisomerisation of other compounds such as (*E*)- and (*Z*)-1-acetyl-3-(2-furfurylidene)oxindole (*I*, $R^1 = \text{COCH}_3$, $R^2 = \text{X} = \text{H}$), (*E*)- and (*Z*)-3-(5-bromo-2-furfurylidene)oxindole (*I*, $R^1 = R^2 = \text{H}$, $\text{X} = \text{Br}$), (*E*)-3-(5-methyl-2-furfurylidene)-

TABLE II

Photoisomerisation Course for Some Furfurylideneoxindoles *I* (Followed by thin-layer chromatography, 250 W lamp)

| R^1 | R^2 | X | R_F | | % <i>E</i> , after exposure to light, min | | | | | |
|-------------------|-------|------------------------------|----------|----------|---|------|------|------|------|-----------------|
| | | | <i>E</i> | <i>Z</i> | 0 | 3 | 6 | 10 | 15 | 20 ^f |
| H | H | H ^a | 0.23 | 0.46 | 88.0 | 79.2 | 75.6 | 74.8 | 69.5 | 55.5 |
| H | H | Br ^b | 0.26 | 0.49 | 92.4 | 91.8 | 89.7 | 87.7 | 85.7 | 50.4 |
| COCH ₃ | H | H ^c | 0.23 | 0.33 | 81.5 | 74.7 | 69.9 | 66.2 | 59.4 | 46.8 |
| COCH ₃ | H | Cl ^d | 0.60 | 0.70 | 70.7 | 68.4 | 66.7 | 66.4 | 59.6 | 42.3 |
| H | H | NO ₂ ^e | 0.46 | 0.67 | 98.4 | 96.8 | 95.6 | 94.0 | 93.8 | 90.5 |

^a Separation on Silufol, solvent system benzene-ethyl acetate (3 : 1); ^b cyclohexane-ethyl acetate (2.5 : 1); ^c benzene; ^d benzene-ethyl acetate (15 : 2); ^e heptane-ethyl acetate (1 : 3); ^f exposure to UV light.

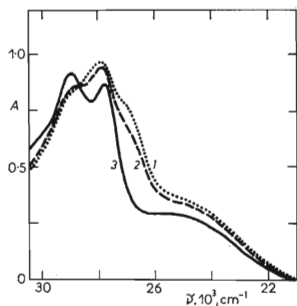


FIG. 2

Photoisomerisation of (*E*)-3-(2-Furfurylidene)oxindole (*I*, $R^1 = R^2 = \text{X} = \text{H}$) in Toluene

In the dark (3); exposure to a light of a 250 W projection lamp, min: 10 (2), 20 (1).

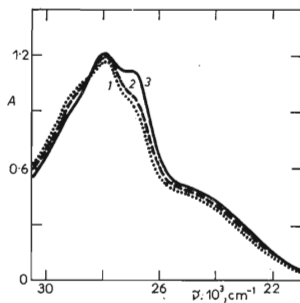


FIG. 3

Photoisomerisation of (*Z*)-3-(2-Furfurylidene)oxindole (*I*, $R^1 = R^2 = \text{X} = \text{H}$) in Toluene

In the dark (3); exposure to a light of a 250 W projection lamp, min: 10 (2), 20 (1).

oxindole (I , $R^1 = R^2 = H$, $X = CH_3$), and (E)-3-(5-methylthio-2-furfurylidene)-oxindole (I , $R^1 = R^2 = H$, $X = SCH_3$) afforded mixtures with approximately equal ratio of isomers, unlike the photoisomerisation of 3-(5-nitro-2-furfurylidene)-oxindole ($R^1 = R^2 = H$, $X = NO_2$).

The course of the photoisomerisation was further followed by semiquantitative thin-layer chromatographic determination of the geometric isomers before and after exposure of solutions of several times crystallised products to light (Table II). Several crystallisations of products obtained from 3-(2-furfurylidene)oxindole (I , $R^1 = R^2 = X = H$), 3-(5-bromo-2-furfurylidene)oxindole (I , $R^1 = R^2 = H$, $X = Br$) and 3-(5-nitro-2-furfurylidene)oxindole (I , $R^1 = R^2 = H$, $X = NO_2$) afforded the more stable E -isomers which contained small amounts of the Z -isomers. However, this procedure failed in cases of 1-acetylfurfurylideneoxindoles (I , $R^1 = COCH_3$, $R^2 = X = H$ and I , $R^1 = COCH_3$, $R^2 = H$, $X = Cl$). Exposure of the solutions of the studied compounds to light led to an equilibrium in which both isomers were approximately equally populated. Again, the derivative I , $R^1 = R^2 = H$, $X = NO_2$ represented an exception: its photoisomerisation gave a mixture in which the E -isomer was the principal component. The photoisomerisation of furfurylideneoxindoles was proved also by 1H -NMR spectroscopy which showed that exposure of a solution of (E)-3-(2-furfurylidene)oxindole (I , $R^1 = R^2 = X = H$) to light afforded a mixture of E - and Z -isomer in the ratio 59 : 41.

The investigation of the photoisomerisation of furfurylideneoxindoles by all the three methods gave identical results and have shown that the geometric isomers of these compounds can be interconverted by the action of light. In all cases the possibility of a thermal isomerisation was excluded.

EXPERIMENTAL

The electronic absorption spectra were measured in toluene solutions on a recording spectrophotometer Specord UV VIS (Zeiss, Jena) in 1 cm cells at room temperature. The 1H -NMR spectra were taken at 25°C on a 80 MHz Tesla BS 487 C instrument in deuteriochloroform using tetramethylsilane as internal standard. The thin-layer chromatographic spots were evaluated semiquantitatively using a Chromoscane (Joyce Loebel) instrument.

The preparation of the substituted furfurylideneoxindoles I was described in our previous paper⁶. The isolated geometric isomers were handled in the dark or in a dim red light.

Isolation of (E)- and (Z)-3-(2-Furfurylidene)oxindoles (I , $R^1 = R^2 = X = H$)

A 5% solution of crude 3-(2-furfurylidene)oxindole (0.63 g; 3 mmol) in dioxane was subjected to thin-layer chromatography ("Silicagel LSL 254 5/40" with 10% plaster, layer thickness 0.3 cm, plates activated for 1 h at 100°C, benzene-ethyl acetate 1 : 3). The separated spots were extracted with ether, the solvent was distilled off *in vacuo* and the obtained isomers crystallised from ethanol. This procedure afforded (E)-3-(2-furfurylidene)oxindole (0.31 g; 49.2%), yellow needles, m.p. 177–178°C, $R_F = 0.23$, and (Z)-3-(2-furfurylidene)oxindole (0.05 g; 7.9%), yellow pasty compound, $R_F = 0.46$.

Photoisomerisation of Furfurylideneoxindoles

A. The separated (*E*)- and (*Z*)-isomers of *I*, $R^1 = R^2 = X = H$, were taken up in toluene, these solutions were exposed to light and their UV spectra were measured at appropriate time intervals. The solutions were photoisomerised in an apparatus in which the diffuse light of a 250 W projection lamp was allowed to pass through a channel and focused on the solution, which was cooled externally with water. In the end of the photoisomerisation the sample was irradiated with UV light. Analogously were photoisomerised: (*E*)- and (*Z*)-*I*, $R^1 = COCH_3$, $R^2 = X = H$, eluant cyclohexane-ethyl acetate (2.5 : 1), and the following *E*-isomers, obtained by several crystallisations of the reaction product: (*E*)-*I*, $R^1 = R^2 = H$, $X = CH_3$; (*E*)-*I*, $R^1 = R^2 = H$, $X = SCH_3$; (*E*)-*I*, $R^1 = R^2 = H$, $X = NO_2$.

B. A 1% dioxane solution of *I*, obtained by several crystallisations of the reaction product, was exposed to light as described under A. At appropriate time intervals a sample was withdrawn and the ratio of *E*- and *Z*-isomers was determined by thin-layer chromatography on Silufol plates (Kavalier, Sázava, Czechoslovakia). This method was used for following the photoisomerisations of *I*, $R^1 = R^2 = X = H$; *I*, $R^1 = R^2 = H$, $X = Br$; *I*, $R^1 = COCH_3$, $R^2 = X = H$; *I*, $R^1 = COCH_3$, $R^2 = H$, $X = Cl$; and *I*, $R^1 = R^2 = H$, $X = NO_2$. The solvent systems and the R_F values of the particular isomers are given in Table II.

C. A methanolic solution (200 ml) of (*E*)-*I*, $R^1 = R^2 = X = H$ (50 mg; 0.25 mmol) was irradiated under nitrogen using an RVK 125 medium-pressure mercury lamp for 3 hours. The solution was taken down *in vacuo*, the residue dissolved in deuteriochloroform and the ratio of *E*- and *Z*-isomers was determined by 1H -NMR spectroscopy.

REFERENCES

1. Staněk J., Rybář D.: Chem. Listy 40, 174 (1946).
2. Hull R., Imperial Chemical Industries Ltd.: Brit. 809 691; Chem. Abstr. 53, 20090 (1959).
3. Hull R., Imperial Chemical Industries Ltd.: U.S. 2 872 372; Chem. Abstr. 53, 13175 (1959).
4. Elliott I. W., Rivers P.: J. Org. Chem. 29, 2438 (1964).
5. Hodges R., Shannon J. S., Jamieson W. D., Taylor A.: Can. J. Chem. 46, 2189 (1968).
6. Kováč J., Štetinová J.: Chem. Zvesti, in press.
7. Ruveda E. A., Gonzales H. A.: Spectrochim. Acta 26 A, 1275 (1970).
8. Daisley R. W., Walker J.: J. Chem. Soc., C, 1971, 3357.
9. Abramovitch R. A., Hey D. H.: J. Chem. Soc. 1954, 1697.
10. Tacconi G., Marinone F.: Ric. Sci. 38, 1239 (1968).

Translated by M. Tichý.