The Photoisomerization Behavior of the (4-Hydroxycinnamoyl)-spermidines

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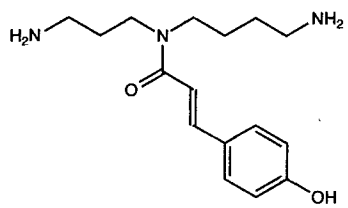
The photoisomerization behavior of three mono[(*E*)-3-(4-hydroxyphenyl)prop-2-enoyl]spermidines, **1**, **2**, and **3**, and three bis[(*E*)-3-(4-hydroxyphenyl)prop-2-enoyl]spermidines, **4**, **5**, and **6**, are investigated. The synthetic product (*E*)-**1** could be almost quantitatively (> 96%) converted into its isomer (*Z*)-**1** under UV light irradiation. In the cases of (*E*)-**2** and (*E*)-**3**, a mixture of (*E*)/(*Z*) *ca.* 1:2 was obtained, when the same conditions were applied. The comparison of their UV spectra provides the possible explanation for these different behaviors. Furthermore, it was noticed that the (*Z*) → (*E*) isomerization of the C=C bond took place during the purification by reverse-phase high-performance liquid chromatography (RP-HPLC), and the (*E*)/(*Z*)-mixture is thus inseparable. The same feature could be observed during the isolation of the (*Z*,*Z*)-*N*,*N*′-bis[3-(4-hydroxyphenyl)prop-2-enoyl]-spermidines, (*Z*,*Z*)-**4**, (*Z*,*Z*)-**5**, and (*Z*,*Z*)-**6**. Nevertheless, the fractions of (*Z*,*Z*)-**5** and (*Z*,*Z*)-**6** were in almost pure state collected, and their ^{1}H-NMR spectra are presented.

Introduction. – Low-molecular-weight phenolic compounds occur in the primary as well as in the secondary cell wall, and they are often linked to cell-wall polymers [1]. The most common of these simple phenolic compounds are the cinnamic acid derivatives, 4-hydroxycinnamic acid (= (*E*)-3-(4-hydroxyphenyl)prop-2-enoic acid) and ferulic acid (= (*E*)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid). These two acids undergo various transitions *in vitro* under the action of light. They both isomerize from the (*E*)- to the (*Z*)-form, and, to a lesser extent, in the reverse direction, to form an equilibrium mixture, in which the (*E*)-form predominates [2–4]. In a quantitative structure-activity relationship study of the antifungal properties of some cinnamic-acid derivatives, it was shown that only (*E*)-isomers are biologically active. Furthermore, the position of the H-atoms at the C=C bond is a key factor for the antifungal property, since the reduction of the C=C bond or interconversion into the (*Z*)-isomer by UV light exposure results in total loss of biological activity [5].

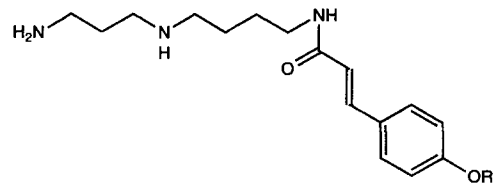
Di- and polyamines can be linked with hydroxycinnamic acids by an amide bond, forming the so-called hydroxycinnamamides (HCAs) [6][7]. The hydroxycinnamamides have now been found throughout the plant kingdom. In a survey of twenty species representing thirteen plant families, HCAs were found to be the main phenolic constituents of the reproductive organs and seeds of all the plants which were analyzed. It is thus generally accepted that HCAs are universal constituents of the reproductive tissues of higher plants. Because of the cinnamoyl chromophores, they undergo (*E*) → (*Z*) isomerization under normal daylight conditions. Several alkaloids bearing a cinnamamide moiety have been isolated from different plant species in both (*E*)- and (*Z*)-forms [8–10]. This photoisomerization behavior has been studied on spermine alka-

[1]) Part of the planned Ph.D. Thesis of *W. H.*, Universität Zürich.

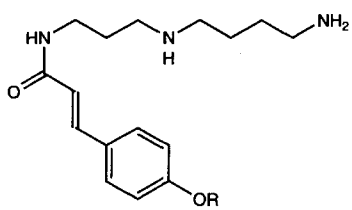
loids containing macrocyclic cinnamoyl moiety. Two new alkaloids, isochaenorpine and isochaenorhine, were obtained by the photoconversion of their natural (*Z*)-forms [11]. The same procedure was applied to implement our strategy to investigate the behavior of (4-hydroxycinnamoyl)-spermidines under UV light irradiation. Recently, the synthesis of seven (*E*)-*N*-[3-(4-hydroxyphenyl)prop-2-enoyl]-spermidines has been accomplished [12]. The aim of this work is to study the isomerization behavior of the pure synthetic (*E*)-compounds and to prepare the corresponding (*Z*)-isomers by exposure to UV light.



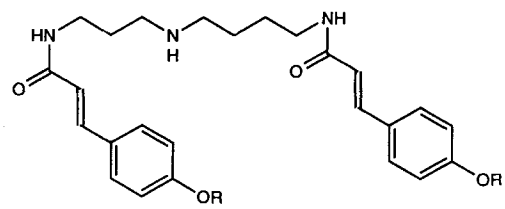
(*E*)-**1**



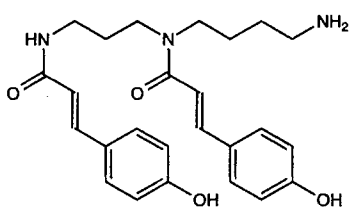
R = H, (*E*)-**2**
R = Me, (*E*)-**7**



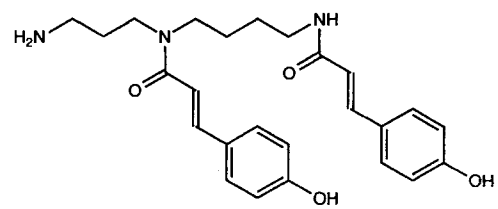
R = H, (*E*)-**3**
R = Me, (*E*)-**8**



R = H, (*E*,*E*)-**4**
R = Me, (*E*,*E*)-**9**



(*E*,*E*)-**5**



(*E*,*E*)-**6**

Results and Discussion. – In general, the photoisomerization of hydroxycinnamic acids or their derivatives is a reversible phenomenon, the final ratio of (*E*)- and (*Z*)-isomers depending on the wavelength of the UV light. According to the scheme

$$(E)\text{-HCAs} \underset{\longleftarrow}{\overset{h\nu}{\rightleftharpoons}} (E)\text{-HCAs}^* \longrightarrow (Z)\text{-HCAs}$$

$$(Z)\text{-HCAs} \underset{\longleftarrow}{\overset{h\nu}{\rightleftharpoons}} (Z)\text{-HCAs}^* \longrightarrow (E)\text{-HCAs}$$

(without discussing the nature of the excited states and the photoisomerization mechanism), a photostationary state is reached when

$$\Phi_{(E)\rightarrow(Z)} \cdot \varepsilon_{(E)} \cdot (1 - \chi_e) = \Phi_{(Z)\rightarrow(E)} \cdot \varepsilon_{(Z)} \cdot \chi_e \quad (1)$$

where $\Phi_{(E)\rightarrow(Z)}$ and $\Phi_{(Z)\rightarrow(E)}$ stand for the $(E) \rightarrow (Z)$ and $(Z) \rightarrow (E)$ isomerization quantum yields, respectively, $\varepsilon_{(E)}$ and $\varepsilon_{(Z)}$ for the extinction coefficients of the (*E*)- and (*Z*)-isomers, respectively, and χ_e for the photostationary molar fraction of the (*Z*)-isomer. Because the extinction coefficients of the phenolic compounds depend on the pH value of the solvent, the final ratio of the (*E*)- and (*Z*)-isomers should also be effected by the pH of the solvent. The photoisomerization is rapid, occurring normally in less than 50 ns [13]. It is O_2-independent and probably occurs *via* a singlet excited state or a very short-lived excited triplet state. In this work, the irradiation was performed with an UV light from 300 to 400 nm with λ_{max} at 350 nm. As no photons in the 280–290 nm region are detectable in the solar spectrum reaching the earth [14], the chosen light covers almost both UV-A (320–380 nm) and UV-B (280–320 nm)[2]) regions. All manipulations of solutions were carried out under red light or in the dark, to prevent any possible unexpected and undesirable light-induced isomerization during workup.

Direct isomerization of the compound (*E*)-**1** was achieved in methanolic solution (10^{-3} M) in a quartz vessel (lamp: *SteriAir BLB-8*). A 15-min irradiation of (*E*)-**1** was sufficient to obtain more than 96% (*Z*)-**1** (confirmed by ^{1}H-NMR spectrum; *Fig. 1, a* and *b*). Because of the hindrance in rotation about N–CO bond, part of the signals was doubled, and a complicated ^{13}C-NMR spectrum was obtained. Surprisingly, the chromatographic purification *via* RP-HPLC led to a (*E*)/(*Z*)-mixture (ratio *ca.* 1:2, by ^{1}H-NMR). Since the light was not involved in this (*E*)/(*Z*)-interconversion, it is assumed that the column material in HPLC could influence the $(E) \rightleftharpoons (Z)$ equilibrium, resulting in inseparable mixtures. (It is well-known that the silica gel has this effect.) *Wasserman et al.* had already noticed some $(Z) \rightarrow (E)$ isomerization during the synthesis of the macrocyclic spermine alkaloid (±)-chaenorhine, which contains a cinnamoyl moiety [15]. The (*E*)/(*Z*)-mixture was inseparable by liquid chromatography. In our case, the liquid chromatography of the pure synthetic (*E*)-isomers using basic eluent system (CH_2Cl_2/MeOH/25% aq. NH_3 78:19:3) led to an (*E*)/(*Z*)-mixture, in which (*E*)-isomers were predominant.

At increased temperature, the hindrance in rotation about the N–CO bond in **1** was overcome, and the spectrum was simplified (*Fig. 1, c*). Under these conditions, no new $(E) \rightarrow (Z)$ isomerization took place. We, therefore, assume that, at least in this case, the $(E) \rightleftharpoons (Z)$ equilibrium is not effected by the temperature (298–333 K). Upon cooling to the room temperature, ^{1}H-NMR spectrum of type *b* (*Fig. 1*) was obtained again, indicating that no other reaction occurred.

The same procedure for the direct isomerization of (*E*)-**1** was applied to (*E*)-**2** and (*E*)-**3**, leading to (*E*)/(*Z*)-mixtures (*ca.* 1:2, by ^{1}H-NMR). After the purification *via* RP-HPLC, (*E*)/(*Z*)-mixtures with almost the same ratios (*ca.* 1:2) were obtained in the supposed (*Z*)-fractions. To rationalize the different photoisomerization behavior of these three isomers, their UV spectra were submitted to analysis.

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[2]) The official definition of the UV-B range was 280–315 nm, established by the *Commission International de l'Eclairage* in 1935.

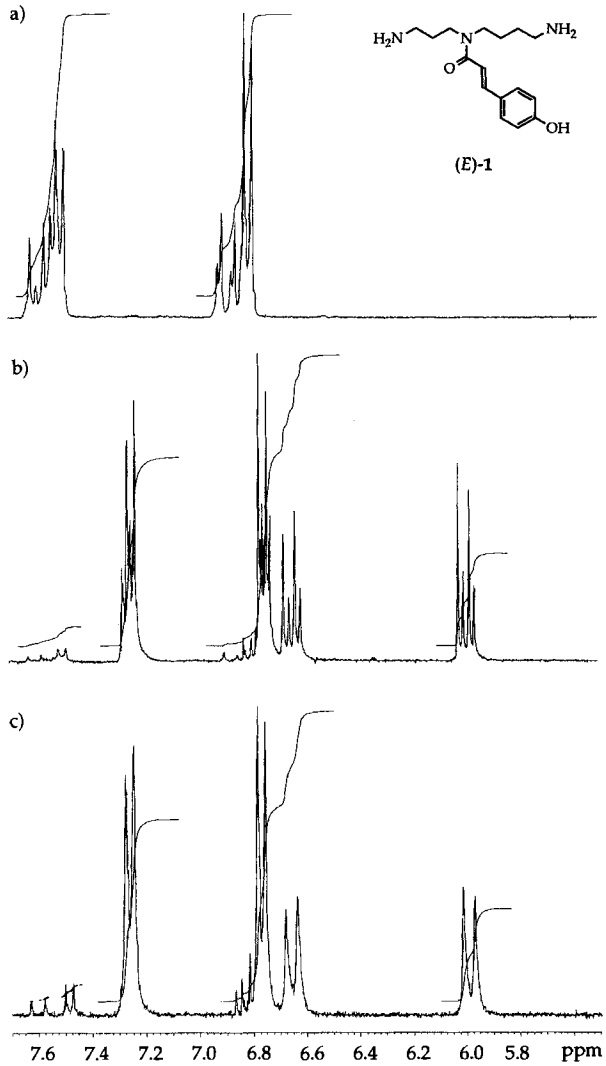


Fig. 1. *Region of the aromatic and olefinic H-atoms in the ^{1}H-NMR spectra* (300 MHz, CD_3OD). *a*) (*E*)-**1** at 298 K; *b*) (*E*)-**1**/(*Z*)-**1** (*ca.* 4: 96) after the exposure to the UV light at 298 K; *c*) (*E*)-**1**/(*Z*)-**1** as in *b*, but at 333 K.

The UV spectra of (*E*)-**1**, (*E*)-**2**, and (*E*)-**3** are shown in *Fig. 2*. The difference between the UV spectra of (*E*)-**1** and (*E*)-**2** or/and (*E*)-**3**, representing the difference between secondary and tertiary amides, was studied in detail by *Grob* and *Fischer* [16].

It was considered that an obvious hindrance in planarity of the 4-hydroxycinnamyl moiety in the disubstituted amides accounts for the difference in the UV spectra of (*E*)-**1** and (*E*)-**2**/(*E*)-**3**. The distinction of the planarities between them could probably be explained by the amide ↔ hydroxyimino tautomerism of (*E*)-**2** and/or (*E*)-**3**, which is missing in (*E*)-**1**, as it is shown in the *Scheme*.

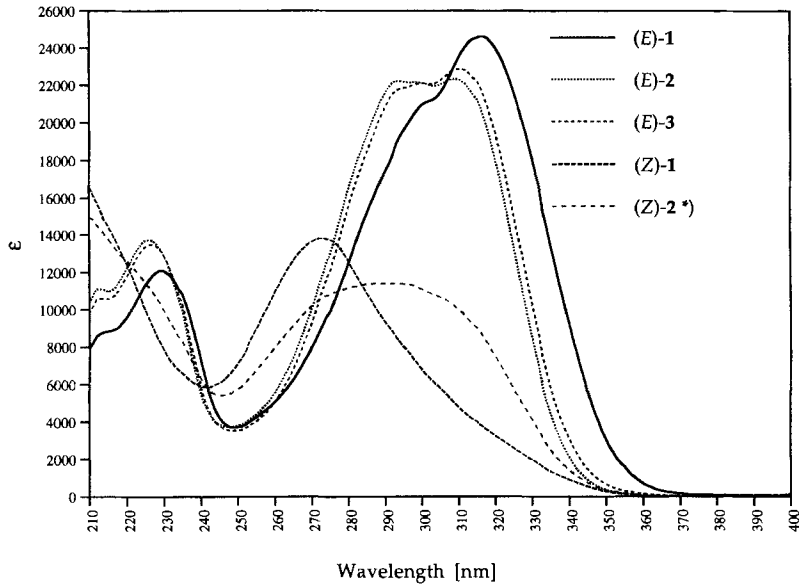
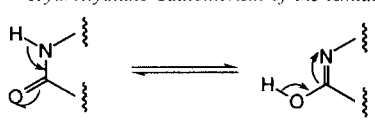


Fig. 2. *UV Spectra of* (E)-**1**, (E)-**2**, (E)-**3**, (Z)-**1**, *and* (Z)-**2** (in EtOH, 10^{-5} M). *) The (*E*)-**2**/(*Z*)-**2** ratio of **2** after the UV light exposure could not be exactly determined by ^{1}H-NMR. The ratio used here was 1:2.

Scheme. *Amide* ↔ *Hydroxyimino Tautomerism of the Amide Bond in* **2** *and* **3**



It is difficult to rationalize the small difference between the UV spectra of (*E*)-**2** and (*E*)-**3**. An 'assumed' approach of the N(4)-atom to the C=O group would lead to a six-membered ring in (*E*)-**3** [17]. With regard to this interaction, the N–CO group in (*E*)-**3** becomes nonplanar [18]. By contrast, there is no interaction between the N(4)-atom and the C=O group in (*E*)-**2**, because of the thus formed energetically less favored seven-membered ring. This difference in constitution between (*E*)-**2** and (*E*)-**3** might cause the small difference in their UV spectra. It must be emphasized that the difference between the UV spectra of (*E*)-**1** and (*E*)-**2** is reproducible by UV detector on HPLC. Therefore, it does not arise from any possible impurity during their syntheses. A similar difference could be observed between the UV spectra of (*E*)-N^8-(4-methoxycinnamoyl)-spermidine (= (*E*)-*N*-{4-[(3-aminopropyl)amino]butyl}-3-(4-methoxyphenyl)prop-2-enamide) and (*E*)-N^1-(4-methoxycinnamoyl)spermidine (= (*E*)-*N*-{3-[(4-aminobutyl)-amino]propyl}-3-(4-methoxyphenyl)prop-2-enamide), the methylated derivatives of (*E*)-**2** and (*E*)-**3**, respectively, as well[1]).

According to *Eqn. 1*, the extent of isomerization depends upon the extinction coefficients of both (*E*)- and (*Z*)-isomers. Thus, to understand the (*E*) ⇌ (*Z*) equilibrium, it is necessary to compare the UV spectra of (*E*)- and (*Z*)-isomers. Since no pure (*Z*)-configurated compounds can be isolated, as it is discussed above, a direct UV measurement

is impossible. The UV spectra can only be obtained by the subtraction of the UV spectra of the (*E*)/(*Z*)-mixture after the direct irradiation from the UV spectra of the synthetically available pure (*E*)-isomers. The (*E*)/(*Z*)-ratio must be determined by ^{1}H-NMR. Compound (*E*)-**1** was almost quantitatively converted into its (*Z*)-isomers and seems ideal for this substraction method.

As it is shown in *Fig. 2*, the intensity at λ_{max} of the UV spectrum of (*Z*)-**1** is almost half of that corresponding to the (*E*)-isomer, and it shows a hypsochromic shift. Computer modelling reveals that the angle between the Ph ring and the C=C bond of the (*Z*)-**1** is *ca.* 60°. This can be explained by the steric repulsions caused by the interaction of the amide group with one of *ortho*-protons of the Ph ring, as it is shown in *Fig. 3* [19]. This distortion strongly reduces the π-orbital conjugation of the 4-hydroxycinnamoyl residue in the (*Z*)-isomers. By contrast, in the (*E*)-isomers the 4-hydroxycinnamoyl moiety is fully conjugated, showing, thus, a much more intensive absorption at a longer wavelength. Comparing the spectra of (*E*)- and (*Z*)-**1**, the two curves overlap at the short-wavelength (< 350 nm) region. Therefore, a total (*Z*) → (*E*) conversion using direct UV light irradiation is impossible.

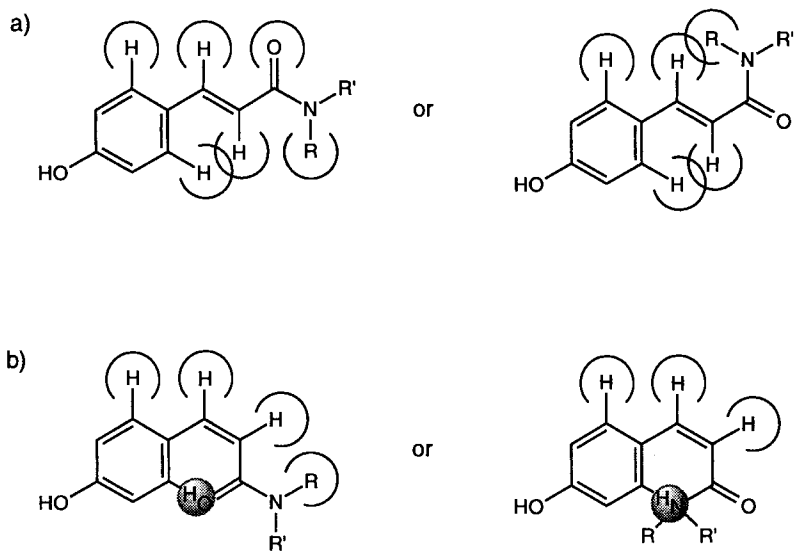


Fig. 3. *Steric interactions in the* a) (E)- *and* b) (Z)-*4-hydroxycinnamoyl moieties*

It must be pointed out that, since the UV and ^{1}H-NMR spectra are of different accuracy, their 'coupling' is, therefore, not always successful. Because the (*E*) → (*Z*)-conversion ratio of **2** and **3** is merely *ca.* $^2/_3$, the exact determination of (*E*)/(*Z*)-ratio by ^{1}H-NMR technique after the direct irradiation is difficult, as it is shown in *Fig. 2*. Thus, the exact UV spectra of the (*Z*)-**2** and (*Z*)-**3** could not be obtained by using this subtraction method. However, the results obtained from the investigation with **1** can be helpful to understand the photoisomerization behavior of **2** and **3**. It is obvious from *Fig. 2* that the overlapping region of the 'uncorrected' UV spectrum of (*Z*)-**2** and (*E*)-**2** is larger than that of (*Z*)-**1** and (*E*)-**1**. By *Eqn. 1*, this explains why more (*E*)-**1** isomerized

to (*Z*)-**1** than (*E*)-**2** to (*Z*)-**2**, using the same UV light irradiation, because $\varepsilon_{(Z)-2}$ is greater than $\varepsilon_{(Z)-1}$ in the region above 300 nm. Though (*Z*)-**2** and (*Z*)-**3** could not be isolated in pure state, the ^{1}H-NMR data for the (*Z*)-isomers can be easily derived from the spectra of the mixture.

The three bis-substituted (4-hydroxycinnamoyl)-spermidines, (*E*,*E*)-**4**, (*E*,*E*)-**5**, and (*E*,*E*)-**6**, display different photoisomerization behaviors as well. Considering the analytical work on the **1**–**3** described above, it is advantageous to have a look at the UV spectra of (*E*,*E*)-**4**, (*E*,*E*)-**5**, and (*E*,*E*)-**6**, before discussing their photoisomerization behavior.

Since the addition of the UV spectra of the synthetic compounds (*E*)-**7** and (*E*)-**8** displays almost exactly the UV spectrum of the compound (*E*)-**9** in EtOH[1]), it is reasonable to assume that the two chromophores in (*E*)-**9** – in this case, the two 4-methoxycinnamoyl moieties – do not interact with each other. Therefore, it is suggested that the UV spectra of the bis-substituted (4-hydroxycinnamoyl)-spermidines can be obtained by adding the UV spectra of the corresponding mono-substituted (4-hydroxyphenyl)-spermidines. This addition method allows us to obtain the UV spectra of the three bis-substituted (4-hydroxycinnamoyl)-spermidines, though the crystallization of (*E*,*E*)-**4**, (*E*,*E*)-**5**, and (*E*,*E*)-**6** failed, and thus their direct UV measurements could not be achieved. Furthermore, with the UV spectra of the bis-substituted (4-hydroxycinnamoyl)-spermidines, a quantitative analysis of the naturally occurring compounds **4**, **5**, and **6** in a mixture by HPLC using UV spectra becomes possible.

After the UV light irradiation of (*E*,*E*)-**4**, a mixture of (*Z*,*Z*)-, (*Z*,*E*)-, (*E*,*Z*)-, and (*E*,*E*)-**4**, are expected. In the HPLC diagram, three signals were observed, which could be assigned to (*Z*,*Z*)-, (*E*,*Z*)- and (*Z*,*E*)-, and (*E*,*E*)-isomers (*Fig. 4*, *a*). On the basis of the analytical work described above for **1**–**3**, it is known that only $^2/_3$ (*E*)-4-hydroxycinnamoyl moieties at N(1) and N(8) isomerized to the corresponding (*Z*)-forms after the irradiation. Regarding the UV spectrum of (*E*,*E*)-**4** as an addition spectrum of the UV spectra of (*E*)-**2** and (*E*)-**3**, and the two chromophores – in this case, the two 4-(hydroxycinnamoyl)moieties – having no interaction with each other, and thus reacting to the irradiation separately, it is reasonable to assume that there are $^4/_9$ (*Z*,*Z*)-**4**, $^2/_9$ (*E*,*Z*)-**4**, $^2/_9$ (*Z*,*E*)-**4**, and $^1/_9$ (*E*,*E*)-**4** in the solution[3]).

By contrast, the (*E*)-N(4)-(4-hydroxycinnamoyl) residue will be isomerized almost quantitatively to its (*Z*)-form under the same conditions. In this case, it can be assumed that there are actually only two compounds, (*Z*,*Z*)- and (*E*,*Z*)-**5** or **6** with a ratio of *ca.* 2:1 in the solution after the irradiation. The very small signal of (*E*,*E*)-**5**, which could arise from (*Z*) → (*E*) isomerization on the HPLC column, supports this assumption (*Fig. 4*, *b*).

The isolation of the compounds (*Z*,*Z*)-**4**, (*Z*,*Z*)-**5**, and (*Z*,*Z*)-**6** were accomplished by the same procedure as for three (*Z*)-mono-substituted (4-hydroxycinnamoyl)-spermidines. It is considerable that the (*Z*,*Z*)-**4** could not be isolated, with regard to (*Z*) → (*E*) isomerization on the column. Therefore, it was surprising that (*Z*,*Z*)-**5** and (*Z*,*Z*)-**6** could

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[3]) Matrix calculation of the isomer ratio in the solution of compound **4** after 15 min UV light irradiation

	$^1/_3$(*E*)-**2**	$^2/_3$(*Z*)-**2**
$^1/_3$(*E*)-**3**	$^1/_9$(*E*,*E*)-**4**	$^2/_9$(*E*,*Z*)-**4**
$^2/_3$(*Z*)-**3**	$^2/_9$(*Z*,*E*)-**4**	$^4/_9$(*Z*,*Z*)-**4**

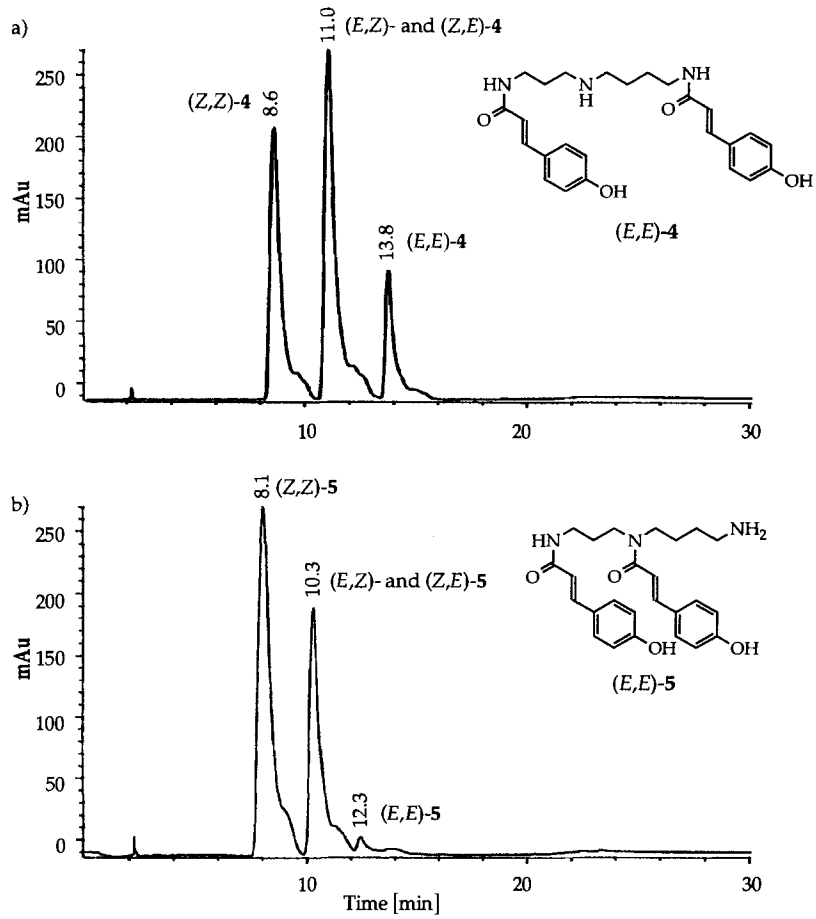

Fig. 4. *HPLC Diagram after 15 min of UV light irradiation of* a) *compound* **4**; b) *compound* **5**

be isolated in nearly pure state. Their ^{1}H-NMR spectra are shown in *Fig. 5*. According to the ^3J values of the protons at the C=C bonds, only a very small part of the (*E*)-isomers – though it is not clear which *N*-(4-hydroxycinnamoyl) moiety they contain – is present.

We cannot explain clearly why (*Z*,*Z*)-**5** and (*Z*,*Z*)-**6** could be isolated, while no (*Z*,*Z*)-**4** was obtained. As a matter of fact, the isolation of the (*Z*,*Z*)-**4** must be more difficult than the isolation of the (*Z*,*Z*)-**5** and (*Z*,*Z*)-**6**, because there are all four possible (*E*/*Z*)-isomers in the solution after the irradiation, while, for compounds **5** and **6**, only two isomers – (*Z*,*Z*)- and (*E*,*Z*)-**5**; (*Z*,*Z*)- and (*Z*,*E*)-**6**, respectively – exist. Further work is necessary to determine whether the different eluent systems and HPLC columns have different effects on the reverse transformation (*Z*) → (*E*) occurring on the column. This could give us the explanation of the different behaviors of **1**–**6** during the preparative HPLC separation.

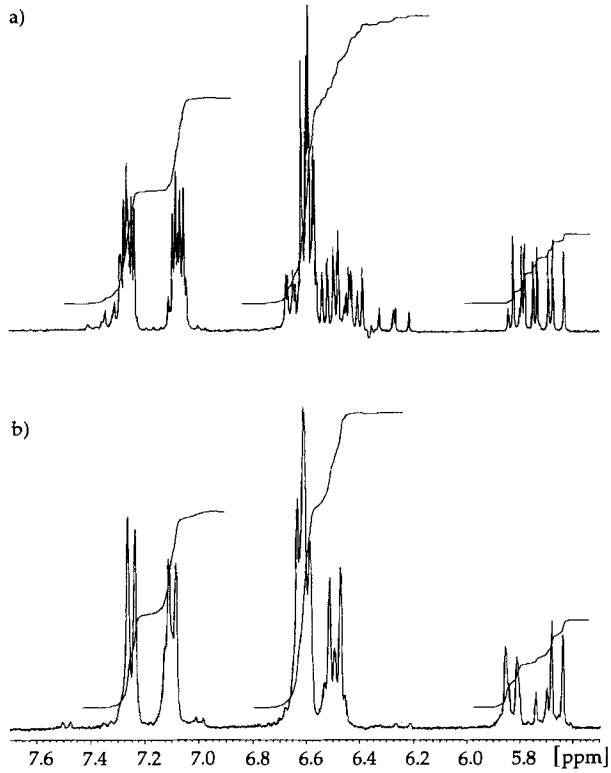

Fig. 5. *Region of the aromatic and olefinic H-atoms in the* ^{1}*H-NMR spectra* (300 MHz, CD_3OD) *of* a) *(Z,Z)*-**5**; b) *(Z,Z)*-**6**

In conclusion, we have described the investigation on the photoisomerization behavior of the (4-hydroxycinnamoyl)-spermidines, and the isolation of their (*Z*)-isomers. Though (*Z*)-**1** was formed almost quantitatively (> 96%) by UV light irradiation, an (*E*)/(*Z*)-mixture (ratio *ca.* 1:2) was obtained after the isolation *via* RP-HPLC. This indicates that a reverse transformation (*Z*) → (*E*) took place on the column, rendering these inseparable mixtures. The different photoisomerization behavior of the mono-substituted (4-hydroxycinnamoyl)-spermidines, (*E*)-**1**, (*E*)-**2**, and (*E*)-**3**, were discussed together with their different UV spectra, which are again affected by their structural properties. Using the UV spectrum addition method, the different photoisomerization behavior of the (*E,E*)-**4**, as compared to (*E,E*)-**5** and (*E,E*)-**6**, could be explained. The preliminary analytical work on bis-substituted (4-hydroxycinnamoyl)-spermidines led to the isolation of the (*Z,Z*)-**5** and (*Z,Z*)-**6.**

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Experimental Part

General. HPLC: *Hewlett-Packard-1090*, equipped with a DAD detector and a *HP-79994A* anal. Workstation (*HP-9000*, modell *300*, *310* desktop computer). The samples were analyzed by HPLC on *Nucleosil* C_8 column (5 μM, 200 × 4 mm i.d.) at a flow rate of 1 ml/min with a two-step linear gradient: in 15 min from 30% solvent *B* (1.5% H_3PO_4, 20% AcOH, 25% MeCN in H_2O) in solvent *A* (1.5% H_3PO_4 in H_2O) to 60% solvent *B* in *A*, and subsequently in 5 min to solvent *B*. Detection at 280 nm. Preparative HPLC was carried out on *Nucleosil 100-7* C_8 with *Perkin-Elmer* series *1 LC* pump and *Perkin-Elmer LC-55B* detector. Detection at 340 nm. UV Spectra: were performed on a *Cary 4* in EtOH. ^{1}H-NMR Spectra: *Bruker ARX-300/AM-300* (300 MHz) in CD_3OD; chemical shifts are given in ppm (*J* in Hz) rel. to CD_3OD. ESI-MS: *Finnigan-SSQ 700*.

1. *(Z)-*N*-(4-Aminobutyl)-*N*-(3-aminopropyl)-3-(4-hydroxyphenyl)prop-2-enamide* ((*Z*)-**1**). A soln. of 20 mg of (*E*)-**1** in 30 ml of MeOH was irradiated with UV light for 15 min by a low-pressure Hg lamp. According to the ^{1}H-NMR spectrum, the mixture contained more than 96% (*Z*)-**1**. The solvent was removed in the dark at r.t., the residue was dissolved again in 0.8 ml of MeOH, and injected into the prep. RP-HPLC (isocratic, 4% MeCN, 3% AcOH in H_2O). The supposed (*Z*)-fractions were combined and freeze-dried in the dark: 19 mg of colorless solid with the (*E*)/(*Z*) ratio of *ca.* 1:2. UV (99% EtOH): see *Fig. 2*. ^{1}H-NMR (CD_3OD, 5 H exchanged, only (*Z*)-isomer, 298 K, *Fig. 1, b*): 7.26, 7.25 (2*d*, *J* = 8.6, 2 arom. H); 6.76, 6.74 (2*d*, *J* = 8.6, 2 arom. H); 6.66, 6.64 (2*d*, *J* = 12.7, 1 olef. H); 6.01, 5.99 (2*d*, *J* = 12.7, 1 olef. H); 3.58–3.37 (*m*, 4 H); 2.07–1.48 (*m*, 6 H). ^{1}H-NMR (CD_3OD, 5 H exchanged, 333 K, *Fig. 2, c*): 7.26 (*d*, *J* = 8.6, 2 arom. H); 6.77 (*d*, *J* = 8.6, 2 arom. H); 6.66 (*d*, *J* = 12.6, 1 olef. H); 5.99 (*d*, *J* = 12.6, 1 olef. H); 3.63–3.34 (*m*, 4 H); 3.07–2.79 (*m*, 4 H); 2.04–1.41 (*m*, 6 H). ESI-MS: 292 ([*M* + 1]$^+$).

2. *(Z)-*N*-{4-[(3-Aminopropyl)amino]butyl}-3-(4-hydroxyphenyl)prop-2-enamide* ((*Z*)-**2**). Analogous to (*Z*)-**1**; from 20 mg of (*E*)-**2** in 20 ml of MeOH, 13 mg of a colorless solid, the (*E*)/(*Z*) ratio of *ca.* 1:2, was obtained after workup. UV (99% EtOH): see *Fig. 2*. ^{1}H-NMR (CD_3OD, 5 H exchanged, only (*Z*)-isomer): 7.42 (*d*, *J* = 8.6, 2 arom. H); 6.74 (*d*, *J* = 8.6, 2 arom. H); 6.66 (*d*, *J* = 12.6, 1 olef. H); 5.84 (*d*, *J* = 12.6, 1 olef. H); 3.41–3.22 (*m*, 2 H); 3.19–2.96 (*m*, 6 H); 2.19–2.03 (*m*, 2 H); 1.83–1.58 (*m*, 4 H). ESI-MS: 292 ([*M* + 1]$^+$).

3. *(Z)-*N*-{3-[(4-Aminobutyl)amino]propyl}-3-(4-hydroxyphenyl)prop-2-enamide* ((*Z*)-**3**). Analogous to (*Z*)-**1**, from 16 mg of (*E*)-**3** in 16 ml of MeOH, 11 mg of a colorless solid, the (*E*)/(*Z*) ratio of *ca.* 1:2, was obtained after workup. ^{1}H-NMR (CD_3OD, 5 H exchanged, only (*Z*)-isomer): 7.43 (*d*, *J* = 8.6, 2 arom. H); 6.75 (*d*, *J* = 8.6, 2 arom. H); 6.71 (*d*, *J* = 12.6, 1 olef. H); 5.87 (*d*, *J* = 12.6, 1 olef. H); 3.45–3.32 (*m*, 2 H); 3.08–2.94 (*m*, 6 H); 2.00–1.65 (*m*, 6 H). ESI-MS: 292 ([*M* + 1]$^+$).

4. *(Z)-*N*-(4-Aminobutyl)-3,3'-bis(4-hydroxyphenyl)-*N,N'*-(propan-1,3-diyl)bis[prop-2-enamide]* ((*Z,Z*)-**5**). A soln. of 30 mg of (*Z,Z*)-**5** in 30 ml of MeOH was irradiated with UV light for 15 min by a low-pressure Hg lamp. The solvent was removed in the dark by r.t., the residue was taken up with 300 μl of MeOH and injected into the prep. RP-HPLC (isocratic, 10% MeCN, 8% AcOH in H_2O). After the separation, the (*Z,Z*)-fractions were combined and freeze-dried in the dark: 15 mg of (*Z,Z*)-**5** as colorless solid. ^{1}H-NMR (CD_3OD, 5 H exchanged, *Fig. 5, a*): 7.41, 7.40 (2*d*, *J* = 8.6, 2 arom. H); 7.23, 7.22 (2*d*, *J* = 8.6, 2 arom. H); 6.75, 6.73, 6.72 (3*d*, *J* = 8.6, 4 arom. H); 6.66, 6.64, 6.57, 6.55 (4*d*, *J* = 12.6, 2 olef. H); 5.94, 5.91, 5.86, 5.80 (4*d*, *J* = 12.6, 2 olef. H); 3.48–3.38 (*m*, 4 H); 3.31–2.77 (*m*, 4 H); 1.91–1.28 (*m*, 6 H): ESI-MS: 438 ([*M* + 1]$^+$).

5. *(Z)-*N*-(3-Aminopropyl)-3,3'-bis(4-hydroxyphenyl)-*N,N'*-(butane-1,4-diyl)bis[prop-2-enamide]* ((*Z,Z*)-**6**). Analogous to (*Z,Z*)-**5**, from 32 mg of (*E,E*)-**6** solved in 30 ml of MeOH, 18 mg of (*Z,Z*)-**6** as colorless solid was obtained after workup. ^{1}H-NMR (CD_3OD, 5 H exchanged, *Fig. 5, b*): 7.37 (*d*, *J* = 8.6, 2 arom. H); 7.23 (*d*, *J* = 8.6, 2 arom. H); 6.75, 6.74 (2*d*, *J* = 8.6, 4 arom. H); 6.67, 6.64 (2*d*, *J* = 12.6, 2 olef. H); 5.98, 5.88, 5.82 (3*d*, *J* = 12.6, 2 olef. H); 3.56–3.40 (*m*, 4 H); 3.26–2.80 (*m*, 4 H); 2.00–1.30 (*m*, 6 H). ESI-MS: 438 ([*M* + 1]$^+$).

6. *Attempted Isolation of (Z)-3,3'-Bis(4-hydroxyphenyl)-*N,N'*-(4-azaoctane-1,8-diyl)bis[prop-2-enamide]* ((*Z,Z*)-**4**). Analogous to (*Z,Z*)-**5**, from 30 mg of (*E,E*)-**4** solved in 30 ml of MeOH, 5 mg of colorless solid was obtained after workup. According to the ^3J values of the protons at the C=C bonds, it is found that in this supposed (*Z,Z*)-fraction the (*E*)-isomers are predominant. No ^{1}H-NMR data of the (*Z,Z*)-**4** could be derived from the spectrum of this mixture. ESI-MS: 438 ([*M* + 1]$^+$).

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