Dyes and Pigments 4 (1983) 59–71

Synthesis and Fluorescence of Some Thiazole and Benzothiazole Derivatives

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(Received: 1 February, 1982)

SUMMARY

The optical properties of a series of thiazole and benzothiazole styryl derivatives are reported. The effect of lengthening the conjugative system in several thiazolyl- and benzothiazolyl-vinyl stilbenes which were prepared and tested as fluorescent whitening agents is discussed.

1. INTRODUCTION

It is known that fluorescent whitening agents are exclusively based on the structures of aromatic and heteroaromatic systems because these are the only systems with configurations which fulfil the essential condition of absorption of short-wave energy by the π electron systems and a re-emission of the absorbed UV energy in the violet to blue spectral range.

Styryl derivatives of heterocycles are a major group of such compounds and a study has been carried out of a series of styrylthiazoles (**Ia** → **c**) and styrylbenzothiazoles (**IIa** → **f**) in their *trans* form.

The styrylthiazole **Ia** is known in the literature.[1] The other members of the series, **Ib, c**, were obtained by the condensation of 2-methylthiazole with the corresponding *para*-substituted benzaldehydes in a sealed tube.

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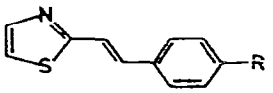
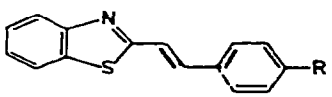
Dyes and Pigments 0143-7208/83/0004-0059/$03·00



Ia → c

Ia: R = H
b: R = Br
c: R = NO_2



II a → f

IIa: R = H
b: R = CH_3
c: R = Cl
d: R = Br
e: R = OCH_3
f: R = NO_2

On the other hand, for the preparation of the styrylbenzothiazoles **IIa → f**, the condensation of ethyl 2-benzothiazolyl acetate with the *para*-substituted benzaldehydes, followed by decarboxylation, was preferred to the synthetic route previously reported for **IIa**,[2] **IIe**[3] and **IIf**[4] starting from 2-methylbenzothiazole because of improved yields. The same procedure, when applied to ethyl 2-benzothiazolyl acetate, was unsuccessful because the condensation did not decarboxylate.

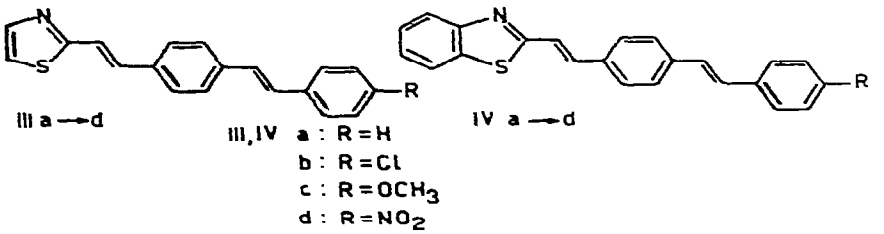
The spectral data of the compounds **I** show that, while for **Ia, b** the emission band occurs at too low a wavelength, for **Ic** it exhibits a maximum in the yellow–orange spectral range. With regard to the benzothiazole derivatives **II**, **IIa → d** emit in the just-visible region, **IIf** exhibits no appreciable fluorescence while **IIe** results in a very good product (see Table 1).

From the data reported in Table 1 it may be concluded that in these molecules simple substitutions of the auxochromic group R are inadequate to obtain compounds with absorption and emission maxima in

TABLE 1
Spectral Data of Thiazole and Benzothiazole Styryl Derivatives **Ia → c** and **IIa → f**

Compound	*Absorption*[a]		Emission[a]
	λ_{max} (*nm*)	$\varepsilon \times 10^{-4}$	λ_{max} (*nm*)
Ia	324	2·75	384
Ib	330	3·20	382
Ic	350	2·80	580
IIa	333	3·16	402
IIb	342	3·63	408
IIc	338	3·46	406
IId	340	3·55	406
IIe	350	3·63	428
IIf	344	3·16	—

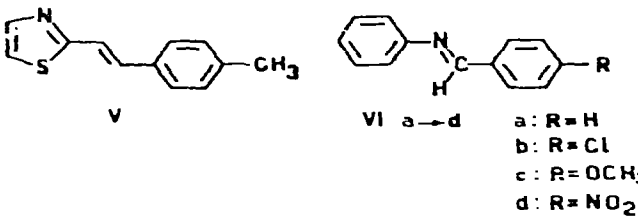
[a] Solutions 10^{-5} M in methanol.



the ranges required for fluorescent whiteners. It therefore seems advisable for this purpose to lengthen the conjugation system of molecules by preparing a series of 4-[β(2-thiazolyl)vinyl]- and 4-[β(2-benzothiazolyl)-vinyl]-stilbene 4'-derivatives **III** and **IV**.

2. RESULTS AND DISCUSSION

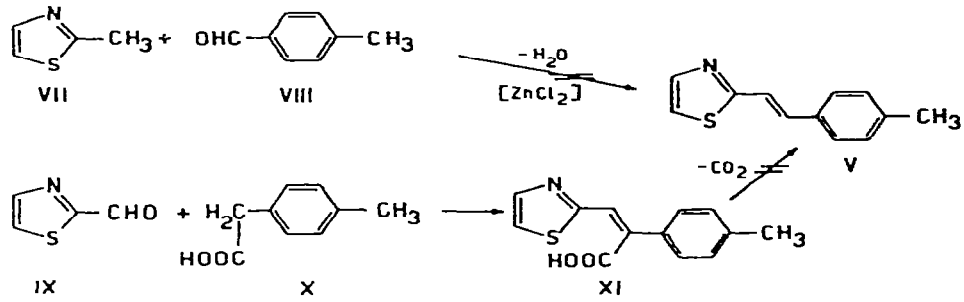
It was hoped to obtain compounds **III** through the 'anil synthesis'[5] between the 2-(*p*-methylstyryl)thiazole **V** and the *N*-phenyl-*para*-substituted benzaldimines **VIa → d**.



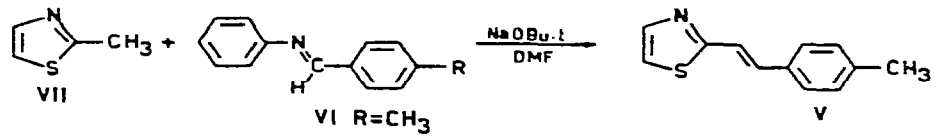
Generally in anil syntheses involving heterocycles, the methyl group is present linked to the nuclei as a *para*-tolyl substituent or, in the case of condensed heterocycles, directly attached to the benzo ring. However, examples of this reaction carried out on *p*-tolylvinyl-pyridines or -benzofurans are also reported.[6,7]

For the preparation of **V** condensation of 2-methylthiazole (**VII**) with *p*-tolylaldehyde (**VIII**) in a sealed tube at 180 °C for 6 h was attempted in the presence of zinc chloride, but reaction did not occur.

Attempts to synthesise compound **V** from 2-thiazolaldehyde (**IX**) and *p*-tolylacetic acid (**X**) were also unsuccessful; α-(*p*-tolyl)-β-(2-thiazolyl)-acrylic acid (**XI**)[8] was obtained in good yield but, unfortunately, it did not undergo decarboxylation by treatment either with $CuCrO_2$ in quinoline or with $Ba(OH)_2$ in ethylene glycol on the boil.

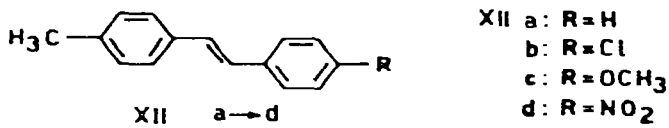


Finally the 2-(*p*-methylstyryl)thiazole **V** was prepared, with low yield, by the reaction between 2-methylthiazole (**VII**) and *N*-phenyl-*p*-methylbenzaldimine (**VI**; $R = CH_3$).



However, compound **V** failed to condense with benzaldimines **VI**, probably due to the lack of reactivity of the methyl group under the required conditions.

Since the 'anil synthesis' also occurs with the anils of heteroaromatic aldehydes,[5] preparation of **III** was attempted by condensation of 2-formylthiazole anil with a series of 4-methylstilbene 4'-derivatives **XIIa → d**.



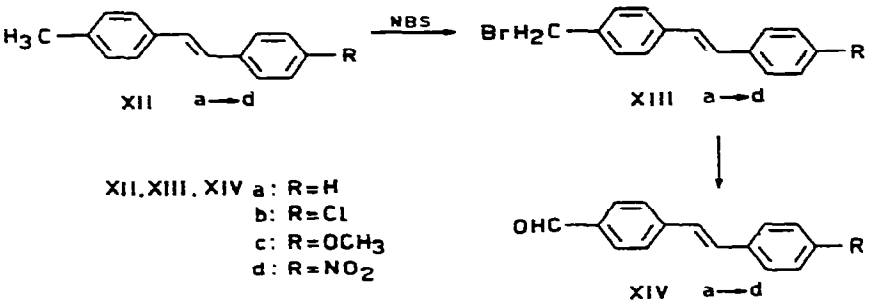
Whereas the other members of the series were obtained by dehydration of the corresponding benzylphenylmethanols,[9] compound **XIId** was prepared by heating *p*-tolylaldehyde (**VIII**) with *p*-nitrophenylacetic acid.[10]

Unfortunately, even by this method it was not possible to obtain the compounds **III**, probably because of the instability of the anils under the reaction conditions.

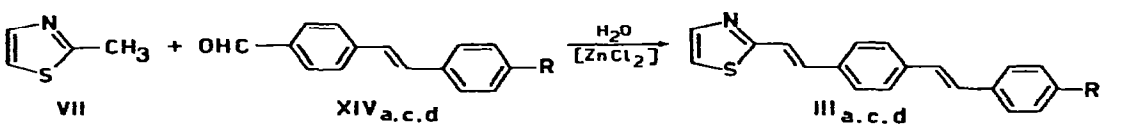
In fact, when 2-formylthiazole anil and **XIIa** were allowed to react at 75 °C for 6 h in DMF and in the presence of sodium *t*-butoxide, we

isolated an unidentified product which, on the basis of analytical data, did not contain nitrogen or sulphur.

In the light of the above results it was thought to obtain the compounds **III** by condensation of 2-methylthiazole **VII** with 4'-substituted 4-stilbenaldehydes **XIVa→d** which were prepared by the Sommelet reaction[11] from **XII**, through the bromomethyl derivatives **XIII**, as in the scheme:



This reaction, reported by Drefahl[12] for compound **XIVa**, was successfully extended both to the yet unknown **XIVb** and to the derivatives **XIVc** and **XIVd** previously obtained by other authors.[13,14] 2-Methylthiazole (**VII**), in the presence of zinc chloride in a sealed tube (see Experimental section), reacted with 4'-substituted 4-stilbenaldehydes to give the vinylstilbenes **IIIa, c, d** in low yields whereas the same reaction was unsuccessful for **XIVb**:



The all-*trans* configuration of compounds **III** was determined by means of their UV spectra, where the conjugation band shows the characteristic vibrational structure and a very high extinction coefficient. The comparison of the longest wavelength band of **IIIa** [360 sh, 368 (4·76), 385 sh] with the one of the *trans–trans* *p*-distyrylbenzene [340 sh, 350 (4·78), 370 sh] is significant.[15]

The fluorescence spectra of compounds **III** show how **IIIa** is a good fluorescent whitening agent while **IIIc** and **IIId** are not suitable because their emission, really very high, occurs at too long a wavelength (Table 2 and Fig. 1).

TABLE 2
Analytical and Spectral Data of 4-[β-(2-thiazolyl)vinyl]stilbenes **IIIa, c, d**

Compound	*M.p.* (°C) *Solvent*	*Yield* (%)	*Formula*	*Analysis*[a]			*Absorption*[b]		*Emission*[b] λ_{max} (*nm*)
				C	*H*	*N*	λ_{max} (*nm*)	$\varepsilon \times 10^{-4}$	
IIIa	219–20	25	$C_{19}H_{15}NS$	78·79	5·33	4·77	368	5·57	438
	n-octane			(78·85	5·22	4·84)			
IIIc	209–10	20	$C_{20}H_{17}NOS$	75·03	5·15	4·08	376	5·25	485
	ligroin			(75·20	5·36	4·39)			
IIId	274–75	30	$C_{19}H_{14}N_2O_2S$	68·23	4·30	8·41	395	4·90	595
	DMF			(68·24	4·22	8·38)			

[a] Values in parentheses refer to the calculated percentages.
[b] Solutions 10^{-6} M in DMF.

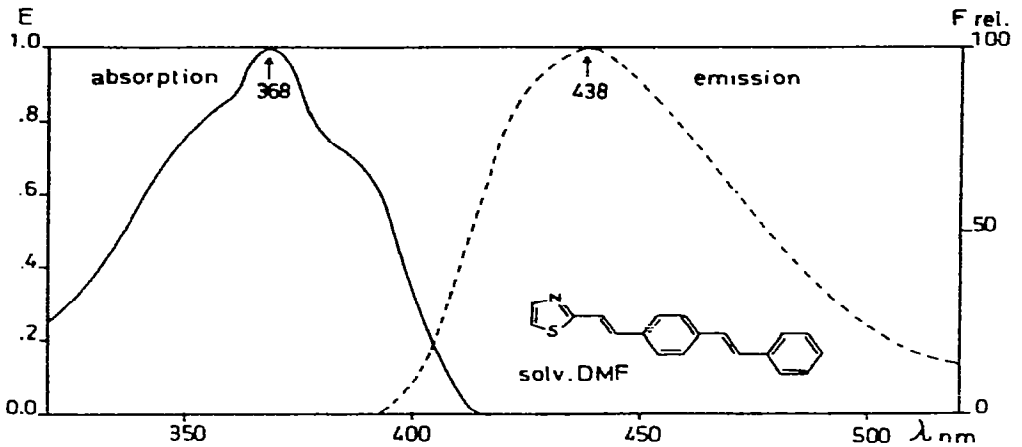
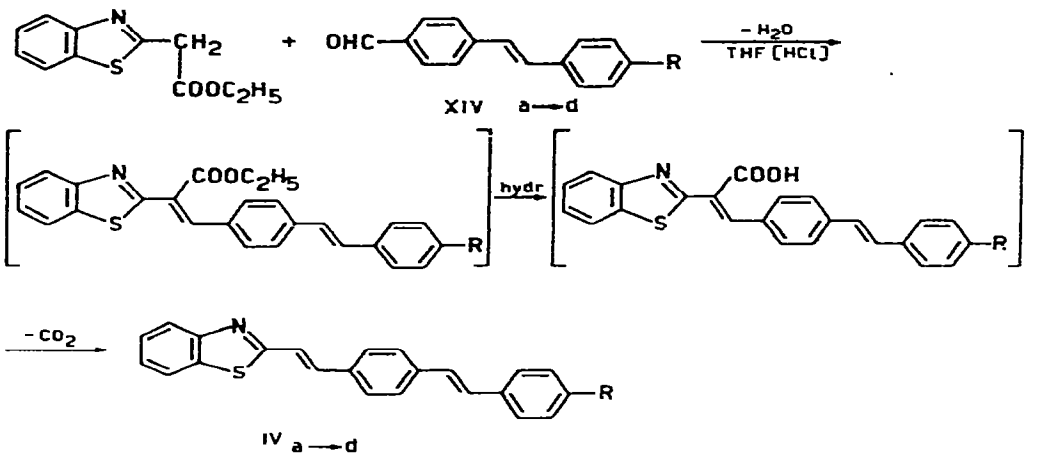


Fig. 1. The adsorption (E) and emission (F) spectra of compound **IIIa**.

The compounds **IVa → d** were synthesised in good yield, likewise the benzothiazole derivatives **II**, by condensation of ethyl 2-benzothiazolylacetate with 4'-substituted 4-stilbenaldehydes **XIVa → d** in the presence of hydrochloric acid in THF as solvent:



Attempts to apply the same method to the thiazole series failed; in fact, as for compounds **II**, the initially isolated condensation products undergo no decarboxylation. From the UV spectral data, with considerations analogous to those for compounds **III**, an all-*trans* structure can be attributed to benzothiazolylvinylstilbenes **IV**.

TABLE 3

Analytical and Spectral Data of 4-[β-2-benzothiazolyl)vinyl]stilbenes IVa→d

Compound	*M.p.* (°C) *Solvent*	*Yield* (%)	*Formula*	*Analysis*[a] (%)			*Absorption*[b]		*Emission*[b] λ_{max} (*nm*)
				C	*H*	*N*	λ_{max} (*nm*)	$\varepsilon \times 10^{-4}$	
IVa	227-28 DMF	63	$C_{23}H_{17}NS$	81·47 (81·38	5·00 5·05	4·16 4·12)	379	6·24	454
IVb	266-68 DMF	45	$C_{23}H_{16}ClNS$	74·02 (73·88	4·22 4·31	3·64 3·75)	382	6·23	454
IVc	300 DMF	70	$C_{24}H_{19}NOS$	78·15 (78·01	5·14 5·18	3·99 3·79)	388	6·23	520
IVd	300 DMF	82	$C_{23}H_{16}N_2O_2S$	72·22 (71·85	4·20 4·19	7·55 7·29)	398	6·31	572

[a] Values in parentheses refer to the calculated percentages.

[b] Solutions 10^{-6} M in DMF.

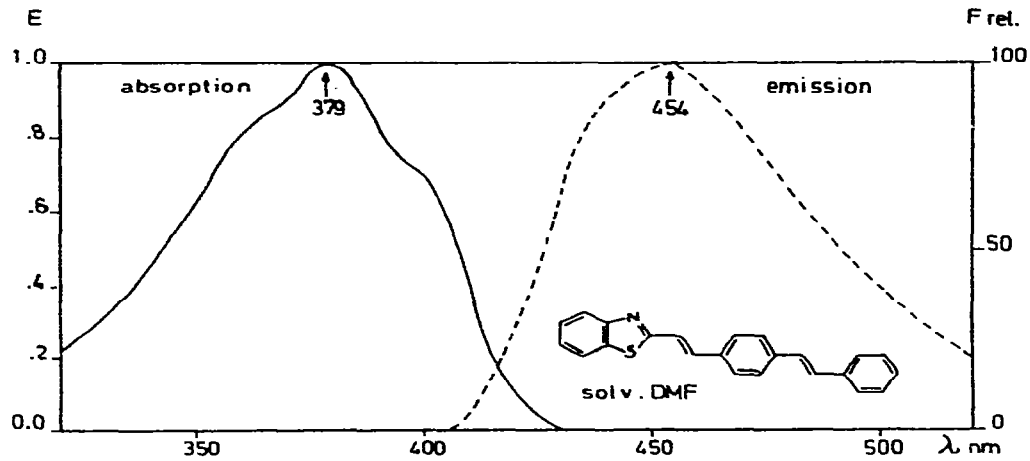


Fig. 2. The absorption (E) and emission (F) spectra of compound **IVa**.

Compounds **IVa** and **IVb** exhibit good fluorescence in the required range while **IVc** and **IVd** show emission bands in the yellow range of daylight (Table 3 and Fig. 2).

The compounds **IIIa**, **IVa** and **IVb** were tested as fluorescent whitening agents on cotton, rayon-viscose and nylon fibres. Each product was dispersed in an aqueous solution of detergent; when the solvent was evaporated, a series of soaps with determined amounts of the testing compounds was obtained. The fluorescent whitening test was carried out using a bath (R.B.1:40) with 2 g/litre of these soaps at 56 °C for 1 h; this procedure was repeated three times per sample.

For the evaluation of whiteness a comparative scale for each fibre was prepared employing the same amounts of a dimorpholine stilbene derivative (CIBA).[16,17] A first analysis shows that, on the treated fibres, compounds **IIIa**, **IVa** and **IVb** give a greater degree of whiteness especially at low concentrations.

3. EXPERIMENTAL

Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer and fluorescence spectra on a Perkin–Elmer MPF-44A spectrophotometer; the maximum of the excitation spectrum is chosen for excitation of the sample. Melting points are uncorrected.

3.1. 2-Styrylthiazoles Ib, c (general procedure)

2-Methylthiazole (0·1 mol) was allowed to react, in a sealed tube at 180 °C for 6 h in presence of 0·1 mol of anhydrous zinc chloride, with 0·1 mol of *p*-bromo- or *p*-nitro-benzaldehyde. The resulting mixture was acidified with 2 N hydrochloric acid (45 ml), filtered and the filtrate extracted with ether to remove the by-products. The acid solution was brought to pH 10 with 2 N sodium hydroxide and extracted several times with ether. Evaporation of the dried (sodium sulphate) extracts gave the required compounds **Ib** and **Ic**.

2-(p-*Bromostyryl*)*thiazole*, **Ib**. M.p. 114–115 °C from light petroleum (b.p. 60–80 °C), yield 21 %. Analysis: Found (%): C, 49·72; H, 3·13; N, 5·23; Calculated for $C_{11}H_8BrNS$: C, 49·63; H, 3·03; N, 5·26.

2-(p-*Nitrostyryl*)*thiazole*, **Ic**. M.p. 206–207 °C from ethanol, yield 38 %. Analysis: Found (%): C, 56·99; H, 3·55; N, 11·79; Calculated for $C_{11}H_8N_2O_2S$: C, 56·89; H, 3·87; N, 12·06.

3.2. 2-Styrylbenzothiazoles IIb, c, d (general procedure)

Concentrated hydrochloric acid (25 ml) was added dropwise at room temperature to a solution of 0·05 mol of ethyl 2-benzothiazolyl acetate and 0·05 mol of the appropriate aldehyde (*p*-tolylaldehyde, *p*-chloro- or *p*-bromo-benzaldehyde) in THF (250 ml). The mixture was heated at 55 °C for 1 h; in these conditions the intermediate ester hydrolysis and the subsequent decarboxylation occur. By cooling, the precipitated crude products were dissolved in water and reprecipitated by addition of potassium carbonate to pH 8.

2-(p-*Methylstyryl*)*benzothiazole*, **IIb**. M.p. 140–142 °C from ethanol, yield 58 %. Analysis: Found (%): C, 76·28; H, 5·28; N, 5·38; Calculated for $C_{16}H_{13}NS$: C, 76·46; H, 5·21; N, 5·57.

2-(p-*Chlorostyryl*)*benzothiazole*, **IIc**. M.p. 173–175 °C from cyclohexane, yield 65 %. Analysis: Found (%): C, 66·12; H, 3·77; N, 4·85; Calculated for $C_{15}H_{10}ClNS$: C, 66·29; H, 3·71; N, 5·15.

2-(p-*Bromostyryl*)*benzothiazole*, **IId**. M.p. 179–180 °C from ligroin, yield 70 %. Analysis: Found (%): C, 56·78; H, 3·23; N, 4·11; Calculated for $C_{15}H_{10}BrNS$: C, 56·97; H, 3·19; N, 4·43.

3.3. 2-(*p*-Methylstyryl)thiazole V

Dimethylformamide (150 ml) was added dropwise at room temperature to a mixture of 0·025 mol of *N*-(*p*-methylbenzyliden)aniline and 0·025 mol of 2-methylthiazole in the presence of 0·06 mol of sodium *t*-butoxide. The solution was then heated at 70 °C for 1 h and, after cooling, filtered.

The filtrate was acidified with 10 % hydrochloric acid to pH 5 and extracted several times with ether.

The combined extracts were dried with sodium sulphate and the solvent evaporated; the distillation of the oily residue gave a product (b.p. 120–125 °C at 0·9 mm Hg) which slowly solidified.

M.p. 88–91 °C, yield 19·5 %. Analysis: Found (%): C, 71·42; H, 5·50; N, 6·77; Calculated for $C_{12}H_{11}NS$: C, 71·60; ; H, 5·50; N, 6·95.

3.4. 4'-Chloro-4-stilbenaldehyde XIVb

4-Methyl-4'-chlorostilbene, **XIIb** (0·03 mol), in 150 ml of carbon tetrachloride, was refluxed for 3·5 h with 0·03 mol of *N*-bromosuccinimide in the presence of 0·2 g of benzoyl peroxide. The succinimide was removed by hot filtration; the filtrate, after cooling, gave a precipitate of 4-bromomethyl-4'-chlorostilbene, **XIIIb**: m.p. 164–165 °C from carbon tetrachloride, yield 54 %.

Analysis: Found (%): C, 58·71; H, 4·06; Calculated for $C_{15}H_{12}BrCl$: C, 58·56; H, 3·93.

Compound **XIIIb** (0·017 mol) in 150 ml of chloroform was refluxed for 2 h with 0·017 mol of hexamethylenetetramine. The precipitated salt, which was separated after cooling and filtering, was again refluxed for 2·5 h with 100 ml of 75 % acetic acid. After cooling, the solid product **XIVb** was filtered and recrystallised.

M.p. 194–195 °C from ethanol, yield 50 %. Analysis: Found (%): C, 74·52; H, 4·35; Calculated for $C_{15}H_{11}ClO$:C. 74·23; H, 4·45.

3.5. 4'-Methoxy-4-stilbenaldehyde XIVc

4-Methyl-4'-methoxystilbene, **XIIc** (0·04 mol), in 150 ml of carbon tetrachloride was refluxed for 3·5 h with 0·04 mol of *N*-bromosuccinimide in the presence of 0·2 g of benzoyl peroxide. After cooling the succinimide

was removed by filtration. When the solvent had been evaporated from the filtrate, 4-bromomethyl-4'-methoxystilbene, **XIIIc**, was obtained.

M.p. 140–142 °C from carbon-tetrachloride, yield 85 %. Analysis: Found (%): C, 63·49; H, 4·97; Calculated for $C_{16}H_{15}BrO$: C, 63·37; H, 4·98.

Compound **XIIIc** (0·03 mol) in 150 ml of chloroform was refluxed for 1 h with 0·03 mol of hexamethylenetetramine. The precipitated salt, which was separated after cooling and filtering, was again refluxed for 3·5 h with 100 ml of 50 % acetic acid. After cooling the solid product **XIVc** was filtered and recrystallised.

M.p. 149–150 °C from acetic acid, yield 52 %. Analysis: Found (%): C, 80·76; H, 6·02; Calculated for $C_{16}H_{14}O_2$: C, 80·68; H, 5·92.

3.6. 4'-Nitro-4-stilbenaldehyde XIVd

4-Methyl-4'-nitrostilbene, **XIId** (0·04 mol), in 150 ml of carbon tetrachloride was refluxed for 5 h with 0·04 mol of *N*-bromosuccinimide in the presence of 0·1 g of benzoyl peroxide. After cooling, the succinimide was removed by filtration. When the solvent had been evaporated from the filtrate, 4-bromomethyl-4'-nitrostilbene, **XIIId**, was obtained.

M.p. 127–129 °C from ligroin, yield 83 %. Analysis: Found (%): C, 56·45; H, 3·93; N, 4·30; Calculated for $C_{15}H_{12}BrNO_2$: C, 56·62; H, 3·80; N, 4·40.

Compound **XIIId** (0·03 mol) in 150 ml of chloroform was refluxed for 1 h with 0·03 mol of hexamethylenetetramine. The precipitated salt, which was separated after cooling and filtering, was again refluxed for 3·5 h with 100 ml of 75 % acetic acid. After cooling, the solid product **XIVd** was filtered and recrystallised.

M.p. 216–219 °C from acetic acid, yield 64 %. Analysis: Found (%): C, 70·92; H, 4·44; N, 5·32; Calculated for $C_{15}H_{11}NO_3$: C, 71·14; H, 4·43; N, 5·55.

3.7. 4-[β-(2-Thiazolyl)vinyl] stilbenes IIIa, c, d (general procedure)

Aldehydes **XIIIa,c,d** (0·1 mol) and methylthiazole **VII** (0·1 mol) were allowed to react in a sealed tube at 180 °C for 6 h in the presence of 0·1 mol of anhydrous zinc chloride. The resulting mixture was acidified with 2 N hydrochloric acid (60 ml), filtered and the filtrate extracted with ether to

remove the by-products. The aqueous acid solution was adjusted to pH 10 with 2 N sodium hydroxide and extracted several times with hot chloroform. The solution was dried with calcium chloride and the solvent evaporated.

3.8. 4-[β-(2-Benzothiazolyl)vinyl] stilbenes IVa → d (general procedure)

Concentrated hydrochloride acid (25 ml) was added dropwise at room temperature to a solution of 0·05 mol of aldehydes **XIVa → d** and 0·05 mol of ethyl 2-benzothiazolylacetate in THF (250 ml). The mixture was heated at 55 °C for 1 h; in these conditions the intermediate ester hydrolysis and the subsequent decarboxylation occur. By cooling, the precipitated crude products were dissolved in water and reprecipitated by addition of potassium carbonate.

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