

## 2-STYRYLBENZOXAZOLE DERIVATIVES

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Received January 16th, 1980

A series of 35 derivatives of 2-styrylbenzoxazole I—XXXV with methyl, chloro, hydroxy, methoxy, dimethylamino, nitro, cyano and methoxycarbonyl substituents have been prepared by reaction of substituted 2-acetamidophenol with respective benzaldehyde derivatives.

Various substituted 2-styrylbenzoxazole derivatives are used as dispersed brightening agents and potentiators of sensibilization of photographic emulsions. They are prepared by condensation of methyl 3-(4-carboxyphenyl)-2-propenate with 1,2-aminophenol and its derivatives<sup>1</sup>, by the Knoevenagel condensation of aromatic aldehydes with benzoxazole derivatives<sup>2</sup>, and by reaction of 2-arylalkylbenzoxazoles with anils of aromatic aldehydes<sup>3</sup>.

We have prepared a series of 2-(4'-R<sup>3</sup>-styryl)benzoxazoles I—XXXV with various substituents and with no, one, or two methyl group(s) at 5 and/or 6 positions of benzoxazole ring system which are not described or incompletely described in patent literature (VII, XII, XIV, XV, XIX, XXI, XXVIII, XXIX). For their preparation a new procedure was found consisting in modification of the Knoevenagel reaction using 2-acetamidophenol instead of the respective benzoxazole for the condensation<sup>4</sup>. All the condensations were carried out in the presence of ammonium dodecylbenzenesulphonate as the condensation agent, because it proved to give the best reaction course and yields out of all the condensation agents investigated by us (zinc dichloride, potassium hydroxide, sodium toluenesulphonate). This procedure was used for condensation of benzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-dimethylaminobenzaldehyde, 4-methoxycarbonylbenzaldehyde, or 4-nitrobenzaldehyde with 1,2-aminophenol to give 2-styrylbenzoxazoles I—VIII. The same aldehydes condensed with 2-acetamido-4-methylphenol gave 5-methyl-2-styrylbenzoxazoles IX—XVI, with 2-acetamido-5-methylphenol they gave 6-methyl-2-styrylbenzoxazoles XVII—XXII, with 2-acetamido-4,5-dimethylphenol they gave 5,6-dimethyl-2-styrylbenzoxazoles XXIII—XXX, and with 2-acetamido-4-methoxyphenol they gave 5-methoxy-2-styrylbenzoxazoles XXXI—XXXV. The starting substances for the syntheses of 2-styrylbenzoxazole derivatives and elemental analyses are given in Table I.

TABLE I  
Starting Substances, Elemental Analyses, and Yields of 2-Styrylbenzoxazoles

Compound 4-R-benzaldehyde	M.p., °C yield, %	Formula (m. mass)	Calculated/Found		
			% C	% H	% N
From acetamidophenol					
<i>I</i>	82—83	$C_{15}H_{11}NO$	81.43	5.01	6.33
H	45	(221.3)	81.31	4.90	6.45
<i>II</i>	192—193	$C_{15}H_{11}NO_2$	75.93	4.67	5.90
HO	18	(237.3)	74.85	4.66	6.01
<i>III</i>	138—139	$C_{16}H_{13}NO_2$	76.47	5.22	5.57
CH <sub>3</sub> O	81	(251.3)	76.30	5.07	5.57
<i>IV</i>	148—149	$C_{15}H_{10}ClNO$	70.55	3.94	5.38 <sup>a</sup>
Cl	82	(255.7)	70.02	4.03	5.20
<i>V</i>	175-176	$C_{17}H_{16}N_2O$	77.25	6.10	10.60
(CH <sub>3</sub> ) <sub>2</sub> N	48	(264.3)	77.95	6.48	10.65
<i>VI</i>	198—199	$C_{16}H_{10}N_2O$	78.03	4.09	11.38
CN	73	(246.3)	77.93	4.09	11.30
<i>VII</i>	166—167 <sup>b</sup>	$C_{17}H_{13}NO_3$	73.11	4.68	5.02
CH <sub>3</sub> OCO	79	(279.3)	73.25	5.05	5.08
<i>VIII</i>	245—246	$C_{15}H_{10}N_2O_3$	67.66	3.79	10.52
NO <sub>2</sub>	81	(226.3)	67.52	3.77	10.07
From 2-acetamido-4-methylphenol					
<i>IX</i>	92—93	$C_{16}H_{13}NO$	81.68	5.57	5.95
H	33	(235.3)	81.99	5.90	5.84
<i>X</i>	228—229	$C_{16}H_{13}NO_2$	76.47	5.22	5.57
HO	63	(251.3)	76.11	5.58	5.38
<i>XI</i>	116—117	$C_{17}H_{15}NO_2$	76.96	5.70	5.28
CH <sub>3</sub> O	73	(265.3)	76.48	5.46	5.24
<i>XII</i>	156—157 <sup>c</sup>	$C_{16}H_{12}ClNO$	71.35	4.49	5.20
Cl	54	(269.7)	71.39	4.67	4.71
<i>XIII</i>	177—178	$C_{18}H_{18}N_2O$	77.67	6.52	10.07
(CH <sub>3</sub> ) <sub>2</sub> N	54	(278.2)	77.67	6.95	10.10
<i>XIV</i>	200—201 <sup>d</sup>	$C_{17}H_{12}N_2O$	78.44	4.65	10.76
CN	80	(260.3)	78.29	4.69	10.69
<i>XV</i>	162—163	$C_{18}H_{15}NO_3$	73.70	5.15	4.78
CH <sub>3</sub> OCO	68	(293.3)	73.67	5.39	4.85
<i>XVI</i>	203—204	$C_{16}H_{12}N_2O_3$	68.56	4.32	10.00
NO <sub>2</sub>	81	(280.3)	68.55	4.63	9.89

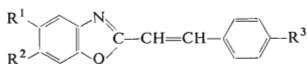
TABLE I  
 (Continued)

Compound	M.p., °C yield, %	Formula (m. mass)	Calculated/Found		
			% C	% H	% N
From 2-acetamido-5-methylphenol					
<i>XVII</i>	77—79	$C_{16}H_{13}NO$	81.68	5.57	5.95
H	27	(235.3)	80.98	5.84	5.93
<i>XVIII</i>	123—124	$C_{17}H_{15}NO_2$	76.96	5.70	5.28
CH <sub>3</sub>	67	(265.7)	76.49	5.58	5.50
<i>XIX</i>	157—158 <sup>f</sup>	$C_{16}H_{12}ClNO$	71.30	4.49	5.20
Cl	78	(269.7)	71.36	4.78	5.58
<i>XX</i>	172—173	$C_{18}H_{18}N_2O$	77.67	6.52	10.07
(CH <sub>3</sub> ) <sub>2</sub> N	50	(278.3)	77.21	6.92	9.75
<i>XXI</i>	148—9	$C_{18}H_{15}NO_3$	73.71	5.15	4.78
CH <sub>3</sub> OCO	66	(293.3)	74.12	5.44	4.80
<i>XXII</i>	188—189	$C_{16}H_{12}N_2O_3$	68.56	4.32	10.00
NO <sub>2</sub>	74	(280.3)	68.12	4.07	10.04
From 2-acetamido-4,5-dimethylphenol					
<i>XXIII</i>	139—140	$C_{17}H_{15}NO$	81.90	6.06	5.62
H	54	(249.3)	81.68	6.22	5.52
<i>XXIV</i>	244—245	$C_{17}H_{15}NO_2$	76.96	5.70	5.28
HO	87	(265.3)	76.96	5.66	5.20
<i>XXV</i>	160—161	$C_{18}H_{17}NO_2$	77.39	6.13	5.01
CH <sub>3</sub> O	80.4	(279.3)	77.16	5.89	4.93
<i>XXVI</i>	183—184	$C_{17}H_{15}ClNO$	72.00	4.97	4.94 <sup>g</sup>
Cl	89	(287.8)	71.80	5.13	4.86
<i>XXVII</i>	242—243	$C_{19}H_{17}N_2O$	78.05	6.90	5.98
(CH <sub>3</sub> ) <sub>2</sub> N	77	(292.4)	78.02	7.16	9.56
<i>XXVIII</i>	196—197	$C_{18}H_{16}N_2O$	78.81	5.14	10.21
CN	74	(274.3)	79.08	5.34	10.14
<i>XXIX</i>	202—203	commercial product Hostaluxe ET			
CH <sub>3</sub> OCO	72				
<i>XXX</i>	240—241	$C_{17}H_{15}N_2O_3$	69.37	4.80	9.52
NO <sub>2</sub>	82	(294.3)	69.32	5.18	9.67

TABLE I  
(Continued)

Compound 4-R-benzaldehyde	M.p., °C yield, %	Formula (m. mass)	Calculated/Found		
			% C	% H	% N
From 2-acetamido-4-methoxyphenol					
XXXI	91—92	C <sub>16</sub> H <sub>13</sub> NO <sub>2</sub>	76.47	5.22	5.57
H	30	(251.3)	76.47	5.22	5.57
XXXII	133—134	C <sub>17</sub> H <sub>15</sub> NO <sub>3</sub>	72.58	5.37	4.98
CH <sub>3</sub> O	83	(281.3)	71.67	5.51	4.87
XXXIII	137—138	C <sub>16</sub> H <sub>12</sub> ClNO <sub>2</sub>	67.35	4.23	4.90 <sup>b</sup>
Cl	88	(285.7)	67.10	4.34	5.10
XXXIV	198—199	C <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O	73.90	4.38	10.14
CN	35	(276.3)	73.61	4.63	10.04
XXXV	166—167	C <sub>18</sub> H <sub>15</sub> NO <sub>3</sub>	69.89	4.89	4.53
CH <sub>3</sub> OCO	91	(309.3)	69.50	5.01	4.51

<sup>a</sup> Calculated: 13.87% Cl; found: 13.78% Cl; <sup>b</sup> ref. m.p. 170°C; <sup>c</sup> ref. m.p. 154—155°C, calculated: 13.16% Cl; found: 13.10% Cl; <sup>d</sup> ref. m.p. 186—197°C; <sup>e</sup> ref. m.p. 159—161°C; <sup>f</sup> ref. m.p. 154 to 155°C, calculated: 13.16% Cl; found: 13.08% Cl; <sup>g</sup> calculated: 12.48%, Cl; found: 12.54% Cl, <sup>h</sup> calculated: 12.41% Cl; found: 12.91% Cl.



- I; R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H  
 II; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = OH  
 III; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = OCH<sub>3</sub>  
 IV; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = Cl  
 V; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = N(CH<sub>3</sub>)<sub>2</sub>  
 VI; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = CN  
 VII; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = COOCH<sub>3</sub>  
 VIII; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = NO<sub>2</sub>  
 IX; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = R<sup>3</sup> = H  
 X; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = OH  
 XI; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = OCH<sub>3</sub>  
 XII; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = Cl  
 XIII; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = N(CH<sub>3</sub>)<sub>2</sub>  
 XIV; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = CN  
 XV; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = COOCH<sub>3</sub>  
 XVI; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = NO<sub>2</sub>  
 XVII; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = H  
 XVIII; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = OCH<sub>3</sub>  
 XIX; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = Cl  
 XX; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = N(CH<sub>3</sub>)<sub>2</sub>  
 XXI; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = COOCH<sub>3</sub>  
 XXII; R<sup>1</sup> = H, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = NO<sub>2</sub>  
 XXIII; R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = H  
 XXIV; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = OH  
 XXV; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = OCH<sub>3</sub>  
 XXVI; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = Cl  
 XXVII; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = N(CH<sub>3</sub>)<sub>2</sub>  
 XXVIII; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = CN  
 XXIX; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = COOCH<sub>3</sub>  
 XXX; R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = NO<sub>2</sub>  
 XXXI; R<sup>1</sup> = OCH<sub>3</sub>, R<sup>2</sup> = R<sup>3</sup> = H  
 XXXII; R<sup>1</sup> = OCH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = OCH<sub>3</sub>  
 XXXIII; R<sup>1</sup> = OCH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = Cl  
 XXXIV; R<sup>1</sup> = OCH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = CN  
 XXXV; R<sup>1</sup> = OCH<sub>3</sub>, R<sup>2</sup> = H, R<sup>3</sup> = COOCH<sub>3</sub>

Most intermediates were obtained by procedures given in literature. 2-Acetamido-5-methylphenol was prepared by nitration of *m*-cresol, subsequent reduction, and acetylation. The nitration procedure given in literature<sup>5</sup> was simplified, the reduction was carried out with sodium dithionite<sup>6</sup> with simultaneous acetylation of the aminophenol formed. 2-Acetamido-4-methylphenol and 2-acetamido-4,5-dimethylphenol were prepared by coupling of benzenediazonium chloride with *p*-cresol and 3,4-dimethylphenol, respectively, in the presence of sodium carbonate<sup>8</sup> (instead of sodium hydroxide<sup>7</sup>). The obtained azo dyestuffs were reduced with sodium dithionite in alkaline medium, the formed aminophenol being simultaneously acetylated<sup>6</sup>. The reductions with zinc in acid medium given in refs<sup>9,10</sup> give impure products in low yields.

## EXPERIMENTAL

### 2-Styrylbenzoxazole Derivatives

Solution of 5 g dodecylbenzenesulphonic acid (Abeson K), 8 ml 1,2-dichlorobenzene and 2 ml aqueous ammonia was treated with 0.55 mol respective aromatic aldehyde and 0.05 mol respective acetylaminophenol. The formed suspension was stirred and heated to 204°C within 30 min during which period about 4 ml water was distilled off. After all water was removed, 20 ml ethanol was added at 90°C. This procedure was applied for preparation of the compounds *II* to *VIII*, *X*—*XXX*, *XXXII*—*XXXV*. Due to different solubility of some products it was necessary to adopt another isolation procedure. For isolation of *I* the product was dissolved by addition of 50 ml butanol at 130°C, and the solution was concentrated to crystallization of *I*. The compound *IX* was separated by cooling at 0°C, the product was collected by suction and washed with ethanol. For preparation of *XXXI* the reaction mixture was cooled and diluted with water. The crystals separated overnight were collected by suction. For elemental analysis the compounds were crystallized from ethanol, except for the compounds *VIII*, *XVI*, *XXII* which were crystallized from chlorobenzene, and except for *XXVII* and *XXX* which were purified by precipitation of their chloroform solutions with ethanol.

### 3-Methyl-6-nitrophenol

Solution of 324.5 g freshly distilled *m*-cresol in 325 g acetic acid was added drop by drop (4 h) into a mixture of 886 ml acetic acid and 333 ml nitric acid (68%) in such way that the temperature did not exceed -10°C. After mixing the both solutions, the mixture was poured onto 2300 g ice and 3500 ml water. The separated oil was removed, and the aqueous layer was extracted with ether. The extracts were combined with the oil portion, and the mixture was steam-distilled. The oily distillate gave 167 g (36%) 3-methyl-6-nitrophenol.

### 2-Acetamido-5-methylphenol

A mixture of 167 g raw 3-methyl-6-nitrophenol, 240 g NaOH, and 2400 ml water was heated to boiling, and the suspension was treated with 570 g sodium dithionite added within 2 h. Red colour of the mixture changed to yellow-green, and the suspension was diluted with water to the volume of 3000 ml; after addition of 2 spoon-ful of charcoal the suspension was hot filtered.

The filtrate was treated with 70 ml conc. hydrochloric acid (weak reaction on the Brilliant yellow paper indicator), and the amino derivative precipitated at 45°C was collected by suction and was washed with small amount of water. The filter cake was mixed with 1000 ml water and dissolved by acidification with conc. hydrochloric acid. The solution was treated with 2 spoon-ful of charcoal and filtered, the light yellow-green filtrate was treated with 150 ml acetanhydride. The mixture was neutralized by addition of sodium carbonate to neutral reaction (Congo red paper indicator negative). The suspension was filtered at 20°C, the filter cake was washed with 250 ml water and dried to give 89 g product (38%), m.p. 155—156°C.

#### 2-Hydroxy-5-methylazobenzene

Solution of 113.5 g *p*-cresol, 40 g sodium hydroxide, and 500 ml water was treated with solution of 265 g sodium carbonate in 1000 ml water. After addition of 1000 g ice, the mixture was treated with the solution of benzenediazonium chloride prepared from 93 g aniline, 500 ml conc. HCl 1000 g ice and 70 g NaNO<sub>2</sub>. When the diazo compound disappeared (after 3 h), the formed azo dyestuff was collected by suction, washed well with water, and dried. Yield 208 g (98%).

#### 2-Acetamido-4-methylphenol

The above azo dyestuff (208 g) was suspended in 1500 ml water and 20 g sodium hydroxide at 90°C, and 489 g sodium dithionite was added thereto. The mixture was heated at 95—100°C 30 min, aniline was removed by steam distillation, and the residue was neutralized with conc. HCl (Brilliant yellow paper indicator). The precipitated hydroxyamino compound was collected by suction, dissolved in 1500 ml water and 85 conc. hydrochloric acid, and the solution was filtered after addition of a small amount of charcoal. The filtrate was alkalinized (weak reaction on the Brilliant yellow paper indicator) and immediately treated with 150 ml acetanhydride. The formed suspension was heated to boiling within 1 h, cooled, the precipitate was collected by suction, washed with 200 ml water, and dried; yield 122 g (74% with respect to aniline), m.p. 156—157°C.

*The elemental analyses were carried out in Analytical-Physical Department, Research Institute of Organic Syntheses, Pardubice - Rybitvi under the guidance of Dr L. Synek. The author is indebted to Mr J. Podstata from the same Institute for technical assistance.*

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Translated by J. Panchartek.