Cis-trans Isomerization of Styrylpyrroles by Stray Light

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A series of substituted *N*-methylstyrylpyrroles (H, *p*-Br, *p*-CN, *o,p*-diCl, *m*-CH_3, *m*-CN, *m*-NO_2) were prepared *via* the Wittig reaction of 1-methylpyrrole-2-carboxaldehyde and substituted benzyltriphenylphosphonium bromides. Both *cis* and *trans* isomers were found to be present in the reaction mixture and they were separable by column chromatography in a few cases (H, *p*-Br, *m*-CN, *m*-NO_2). Photochemical isomerizations of *cis*-styrylpyrroles to *trans* isomers were observed when the substituents were *o,p*-diCl and *m*-NO_2, while the opposite was the case with compounds having H, *p*-Br, *m*-CH_3, *m*-CN. It was difficult to separate the *cis* and *trans* mixture of *p*-cyanostyrylpyrroles and the equilibrium ratio did not change under similar photochemical reaction conditions.

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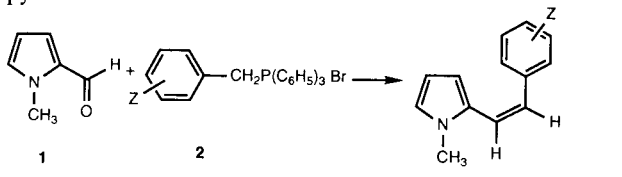
Styryl derivatives of heterocyclic aromatic compounds are of interest because of the remarkable characteristics of their uv spectra and their utility in the synthesis of polycyclic systems [1-4]. For the synthesis of styrylthiophene and styrylfuran the Wittig reaction has been widely employed [5,6]. On the other hand, instances of the reactions of pyrrole-2-carboxaldehyde, which is more conjugative than the furan or thiophene analogues, with the Wittig agents are rare [7]. Jones and Linder reported the formation of a mixture of *cis*- and *trans*-styrylpyrroles *via* the Wittig reaction [8,9]. As a part of our continuing investigation of the reactions of vinyl derivatives of 5-membered heterocyclic compounds we reexamined the synthesis of substituted styrylpyrroles.



1 2 3

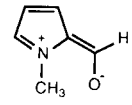
Z

a, H
b, *p*-Br
c, *p*-CN
d, *o,p*-Cl_2
e, *m*-CH_3
f, *m*-CN
g, *m*-NO_2

4

Results and Discussion.

We chose 1-methylpyrrole-2-carboxaldehyde (**1**) instead of pyrrole-2-carboxaldehyde because the N-H compound has quite different chemical properties, compared to the *N*-substituted counterparts [10]. As Wittig reagents substituted benzyltriphenylphosphonium bromides **2** were employed, which, in turn, were prepared from triphenylphosphine and the corresponding benzyl bromides. The yield of styrylpyrroles **3** and **4** were about 20%. The low yield was not surprising because of the contribution of the resonance structure such as **I** [11].



I

Separation of the isomers was usually done by column chromatography (silica gel, petroleum ether-diethyl ether), but mixtures of both isomers were obtained for *p*-bromo **3c** and **4c** (2:1) and *o,p*-dichloro **3d** and **4d** (7:1) compounds.

The structures of styrylpyrroles **3** and **4** were determined by their spectra. One of the characteristics of the ir spectrum of **4** is the appearance of a strong peak at 1620 cm^{-1}. The wagging vibration of the *trans* hydrogens also appears, at around 955 cm^{-1}. In the ^{1}H-nmr spectrum an AB pattern centered at about δ 6.88 and 7.27 with J = 16 Hz is also evidence of the *trans* HC=CH moiety. The bathochromic shift in the uv spectra due to the extension of the conjugation is notable. Thus, λ max value of **4a** is 338 nm, while that of **1** is 270 nm. Comparison of the spectra of **3** and **4** is interesting. The intensity of the peak at 1620 cm^{-1} is the medium in the ir spectrum of **3**. The chemical shift of the singlet due to *N*-CH_3 is about δ 3.67 for the *trans* compounds. An up-field shift to about δ 3.52 is observed in the *cis* compounds **3**. The difference in the λ max values of **3** and **4** is about 10 nm and the *cis* compounds **3** absorbe shorter wavelength in all cases. This is a good evidence of effective conjugation in the *trans* compounds **4**. In **3** the *ortho*-hydrogen of the phenyl ring and C_3-hydrogen atom of pyrrole ring seem to repel each other to prohibit the coplanarity of the two rings. Therefore, the overlapping of the *p*-orbitals is not as much effective as in the *trans* compounds. The distortion of the phenyl ring has been previously shown in *cis*-2-styrylfurans and *cis*-2-styrylthiophenes [12].

One of the interesting observations is the isomerization of the two isomers by light. The uv spectral data are listed in Table I. When a solution of **4a** (10^{-3} *M*) in commercial

Table I

Electronic Absorption Maxima of Styrylpyrroles, λ max (log ε) [a]

Compound	Stock solutions	Commercial ethanol [b]		Purified ethanol [c]	
		Stray light 24 hours	Mercury lamp [d], 5 hours	Stray light 24 hours	Mercury lamp [d], 5 hours
4a	338 (4.44)	325 (4.06)	[e]	333 (4.27)	[e]
3b	337 (3.95)	337 (3.95)	[e]	337 (3.94)	[e]
4b	347 (4.32)	337 (3.95)	[e]	337 (3.90)	[e]
3c [f]	370 (4.20)	369 (4.18)	369 (4.20)	369 (4.10)	369 (4.10)
3d [g]	335 (4.01)	338 (3.94)	340 (3.98)	338 (3.96)	340 (4.00)
4e	333 (4.22)	295 (3.89)	[e]	295 (3.96)	[e]
4f	349 (4.20)	340 (3.94)	[e]	343 (3.99)	[e]
3f	333 (4.00)	337 (4.32)	344 (4.41)	338 (4.09)	344 (4.43)

[a] No change was apparent in all cases under dark for 6 days. [b] E. Merck. Co., Darmstadt, Germany, GR grade absolute ethanol. [c] Distilled over sodium hydroxide. [d] 450 watt medium pressure mercury lamp. [e] Characteristic uv bands of styrylpyrroles disappeared completely. [f] Mixture of **3c** and **4c** (2:1). [g] Mixture of **3d** and **4d** (7:1).

ethanol (reagent grade) was left at room temperature under the stray light for 24 hours λ max was shifted from 338 nm to 325 nm. On the other hand, when the ethanol was distilled over sodium hydroxide before use, the shift was only 5 nm during the same period. Neither unpurified nor purified ethanol solutions of **4a** changed their λ max when kept in the dark for 6 days.

When the purified ethanol solution of **4a** (10^{-1} *M*) was irradiated with a medium pressure mercury lamp for 5 hours the uv spectra of the solution showed only a rising end absorption at 250 nm and neither **4a** nor **3a** was present. This was confirmed by tlc and nmr spectroscopy of the residue after evaporation of the solvent. The residue was a gum which seemed to be a polymer of the styrylpyrrole. Examination of the reaction mixture with the mercury lamp by gas chromatography at various time intervals showed that the rate of disappearance of **4a** was much faster than that of isomerization to **3a**. The nature of this change is uncertain, but similar kind of changes were observed with **4b** (*p*-Br), **4e** (*m*-CH_3), and **4f** (*m*-CN).

On the other hand, the *trans* isomers having strong electron withdrawing groups **4d** and **4g** did not isomerize to the *cis* form **3d** and **3g**, respectively, after the irradiation of their ethanol solution for 5 hours. However, the *cis* compounds, **3d** and **3g**, did isomerize to the *trans* isomers upon irradiation for 5 hours. The photochemical isomerization is apparently facilitated by employing a protic solvent and by the presence of an acidic impurity in the solvent. This was confirmed by employing ethanol containing 1% of acetic acid, in which the isomerization of **4a** to **3a** took place within an hour substantially. The results of the photochemical isomerization of **4a** to **3a** in hexane and in ethanol are listed in Table II. It is clear that the isomerization takes places faster in ethanol. However, the length of the time for reaching isomerization did not show any correlation with the substituents (data not shown). Furthermore, the styrylpyrroles having electron donating substituents on the phenyl ring isomerize from the *trans* to the *cis* form, *eg.* **4b** and **4e** to **3b** and **3e**, respectively, under stray light, while the others do not. Compound **4f** (*m*-CN) is somewhat unusual in that it undergoes isomerization to **3f** although *m*-CN is considered to be an electron-withdrawing substituent.

In most cases except *m*-CH_3, **4e** and *p*-CN, **4c** the isomerization was usually over 85% completion (confirmed by gc and nmr). In case of *m*-CH_3 the *trans* isomer **4e** changed to the *cis* isomer **3e** but further reaction such as polymerization took place quite rapidly and therefore, **3e** was not present at all after the 6 days under stray light.

Table II

Percent Conversion of **4a** to **3a** under Stray Light at 25° in a Pyrex Flask [a,b]

Hour	Hexane			Ethanol	
	Sealed	Nitrogen [c]	Oxygen [c]	Absolute	1% Acid [d]
0	0	0	0	0	1.8
1	3.7	3.4	3.9	9.7	14.7
3	14.4	19.0	18.4	21.6	31.0
6	27.2	28.3	26.8	49.9	56.8
12	33.1	32.7	31.4	68.7	86.6
24	45.2	47.3	46.3	76.8	87.2
48	83.2	81.6	76.3	76.8	88.3
72	87.5	86.5	85.3	87.6	88.3
96	88.3	86.5	87.7	88.5	89.6
144	88.7	88.0	88.0	88.6	89.9

[a] The volume of each reacting solution was 10 ml and the concentration of the solution was 10^{-3} *M*. [b] No change took place under dark after 6 days. [c] The gas was bubbled into the solution and fresh solvent was added occasionally to make up the evaporated volume. [d] The solution contained 1% of glacial acetic acid by volume.

EXPERIMENTAL

Melting points were determined on a MEL-TEMP apparatus and uncorrected. Infrared (ir) and ultraviolet and visible (uv) spectra were recorded on Perkin-Elmer Models 783 and 552-S spectrophotometers, respectively. Nuclear magnetic resonance (nmr) spectra were recorded on a JEOL FX-90Q FT NMR spectrometer using tetramethylsilane as internal standard. Electron impact mass spectra (ms) were obtained by Kratos MS 25 RFA spectrometer. Gas chromatogram was obtained using a Varian Vista 6000 gas chromatograph equipped with a capillary column (DB-5, 0.25 mm I.D., 30 m) and a flame ionization detector (conditions: initial temperature 120°; initial hold 6 minutes; temperature increase 6°/minute; final temperature 300°). Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona, U.S.A.

Starting Materials.

1-Methylpyrrole-2-carboxaldehyde (**1**) was a purchased commercial product and distilled prior to use. The Wittig agents **2** were prepared by reacting substituted benzyl bromides and triphenylphosphine in benzene.

Styrylpyrroles. Illustrative Procedure: (*Z*) and (*E*)-1-(1-Methyl-2-pyrrolyl)-2-phenylethene **3a** and **4a**.

Sodium (0.57 g, 25 mmoles) was added to absolute ethanol (17 ml) and after the completion of reaction was added benzyltriphenylphosphonium bromide (**2a**, 10.5 g, 25 mmoles). The mixture was stirred for a few minutes and **1** (2.80 g, 25 mmoles) was added dropwise. The resulting mixture was stirred and heated at 50° for 1.5 hours under nitrogen. After evaporation of the solvent to dryness under aspirator pressure water (20 ml) was added and the solution was extracted with ether (3 x 50 ml). The ethereal extract was concentrated and chromatographed on a column of silica gel (1.5 cm x 30 cm, 60-230 mesh) prepared with petroleum ether (30-60°)-diethyl ether (95:5). The same solvent mixture was used for elution: (1) 90 ml; (2) 225 ml; (3) 150 ml. The fraction 1 was **3a** (2.54 g, 55%) which was a pale yellow viscous oil and its structure was confirmed by comparison of its spectra (ir and uv) with literature [8]. Fractions 2 and 3 gave **4a** (0.47 g, 10%), mp 70-73° (lit [8] 70-73°) and its spectra (ir and uv) were identical with literature [8].

(*Z*) and (*E*)-2-(4-Bromophenyl)-1-(1-methyl-2-pyrrolyl)ethene, **3b** and **4b**.

It was difficult to isolate pure form of **4b** by column chromatography. Finally purified **4b** had less than 5% (by nmr) of **3b** as impurity. The crude yield was about 20% of **4b** while the purified yield after three chromatography was about 1%, mp 90-95° (lit [9] 95-96°); ir (potassium bromide): 3450 (water impurity), 1620, 1480, 1460, 1420, 1310, 950, 720 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.67 (s, 3 H, NCH_3), 6.02 (dd, 1 H, 4-H of pyrrole, $J_{4,3}$ = 3.6 Hz, $J_{4,5}$ = 2.7 Hz), 6.47 (dd, 1 H, 3-H of pyrrole, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.6 Hz), 6.77 (dd, 1 H, 5-H of pyrrole, $J_{5,3}$ = 1.6 Hz, $J_{5,4}$ = 2.7 Hz), an AB pattern centered at 6.80 and 7.20 (2 H, HC=CH, J = 16.3 Hz), 7.49 (s, 4 H, C_6H_4).

Anal. Calcd. for $C_{13}H_{12}BrN \cdot 1/2H_2O$ (271.16): C, 57.58; H, 4.83; Br, 29.46; N, 5.16. Found: C, 57.89; H, 4.81; Br, 29.42; N, 5.23.

Compound **3b** was isolated in *ca.* 30% as a gummy liquid; ir (neat): 3090, 1618, 1460, 1413, 1300, 805, 720 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.52 (s, 3 H, NCH_3), 5.94 (m, 1 H, 4-H of pyrrole), 6.42 (m, 1 H, 3-H of pyrrole), 6.77 (m, 1 H, 5-H of pyrrole), an AB pattern centered at 7.28 and 7.42 (2 H, HC=CH, J = 8.0 Hz), 7.49 (s, 4 H, C_6H_4); ms: m/z (%) 263 (98, M^+ +2), 262 (20), 261 (100, M^+), 183 (25), 181 (27), 80 (12), 79 (10).

Anal. Calcd. for $C_{13}H_{12}BrN$ (262.16): C, 59.56; H, 4.61; Br, 30.48; N, 5.34. Found: C, 59.34; H, 4.63; Br, 30.09; N, 5.51.

(*Z*) and (*E*)-2-(4-Cyanophenyl)-1-(1-methyl-2-pyrrolyl)ethene, **3c** and **4c**.

As described in the text **3c** and **4c** were obtained as a 2:1 mixture (45%), mp 73-76°; ir (melt): 2210 (C=N), 1620, 1590, 1480, 1420, 1300, 950, 730 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.55 (s, NCH_3 of **3c**), and 3.70 (s, total 3 H, NCH_3 of **4c**), 5.90-5.92 (m, 1 H, 4-H of pyrrole), 6.20-6.09 (m, 1 H, 3-H of pyrrole), an AB pattern centered at 6.37 and 6.60 (HC=CH of **3c**, J = 12.4 Hz), 6.76-6.80 (m, 1 H, 5-H of pyrrole), an AB pattern centered at 6.89 and 7.39 (HC=CH of **4c**, J = 16.4 Hz), an AB pattern centered at 7.54 and 7.73 (4 H, C_6H_4 of **3c** or **4c**, J = 8.3 Hz), 7.72 (s, 4 H, C_6H_4 of **4c** or **3c**); ms: m/z (%) 208 (100, M^+), 148 (18), 80 (10).

Anal. Calcd. for $C_{14}H_{12}N_2$ (208.26): C, 80.74; H, 5.81; N, 13.45. Found: C, 80.83; H, 6.04; N; 13.19.

(*Z*) and (*E*)-2-(2,4-Dichlorophenyl)-1-(1-methyl-2-pyrrolyl)ethene, **3d** and **4d**.

Upon column chromatography of the reaction mixture a mixture of **3d** and **4d** (7:1 by nmr) was isolated (15%), mp 64-65°; ir (melt): 1620, 1580, 1470, 1420, 1300, 950, 710 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.56 (s, NCH_3 of **3d**) and 3.68 (s, total 3 H, NCH_3 of **4d**), 5.61-5.65 (m, 1 H, 4-H of pyrrole), 5.79-5.86 (m, 1 H, 3-H of pyrrole), an AB pattern centered at 6.24 and 6.65 (HC=CH of **3d**, J = 11.9 Hz), 6.71 (m, 1 H, 5-H of pyrrole), 7.0-8.0 (m, phenyl-H and HC=CH of **4d** with J = 16.0 Hz); ms: m/z (%) 255 (3, M^+ +4), 253 (32, M^+ +2), 251 (100, M^+), 173 (12), 171 (34), 80 (12), 79 (35).

Anal. Calcd. for $C_{13}H_{11}Cl_2N$ (252.14): C, 61.93; H, 4.40; Cl, 28.12; N, 5.55. Found: C, 61.70; H, 4.45; C, 28.20; N, 5.32.

(*E*)-2-(3-Methylphenyl)-1-(1-methyl-2-pyrrolyl)ethene (**4e**).

The yield of this reaction was quite low and none of the *Z* isomer **3e** was isolated. Compound **4e** (7%) had mp 50-55°; ir (melt): 1620, 1480, 1420, 1300, 950, 750, 720 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 2.34 (s, 3 H, Ar-CH_3), 3.67 (s, 3 H, NCH_3), 6.03 (dd, 1 H, 4-H of pyrrole, $J_{4,3}$ = 3.7 Hz, $J_{4,5}$ = 2.7 Hz), 6.47 (dd, 1 H, 3-H of pyrrole, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.8 Hz), 6.76 (dd, 1 H, 5-H of pyrrole, $J_{5,3}$ = 1.8 Hz, $J_{5,4}$ = 2.7 Hz), 7.01 (s, 1 H, 2-H of phenyl), 7.11-7.70 (m, 3 H, 4-, 5-, and 6-H of phenyl); ms: m/z (%) 197 (100, M^+), 117 (35), 91 (56), 80 (10), 79 (12).

Anal. Calcd. for $C_{14}H_{15}N$ (197.28): C, 85.24; H, 7.66; N, 7.10. Found: C, 85.08; H, 7.75; N, 6.89.

(*E*)-2-(3-Cyanophenyl)-1-(1-methyl-2-pyrrolyl)ethene (**4f**).

None of the *Z* form of **3f** was isolated. Compound **4f** (8%) had mp 54-57°; ir (melt): 2220 (C=N), 1630, 1600, 1480, 1420, 1310, 960, 730 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.66 (s, 3 H, NCH_3), 6.00 (m, 1 H, 4-H of pyrrole), 6.13 (m, 1 H, 3-H of pyrrole), 6.52 (m, 1 H, 5-H of pyrrole), 6.0-7.8 (m, 6 H, HC=CH and phenyl-H); ms: m/z (%) 208 (100, M^+), 148 (33), 80 (15).

Anal. Calcd. for $C_{14}H_{12}N_2$ (208.26): C, 80.74; H, 5.81; N, 13.45. Found: C, 80.61; H, 5.93; N, 13.23.

(*Z*) and (*E*)-1-(1-Methyl-2-pyrrolyl)-2-(3-nitrophenyl)ethene, **3g** and **4g**.

Compound **3g** (37%) had mp 50°; ir (melt): 1610, 1570, 1520

(NO_2), 1480, 1415, 1345 (NO_2), 1305, 730 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.57 (s, 3 H, NCH_3), 5.91 (m, 2 H, 3- and 4-H of pyrrole), an AB pattern centered at 6.55 and 6.57 (2 H, HC=CH, J = 12.1 Hz), 6.77 (m, 1 H, 5-H of pyrrole), 7.60 (m, 1 H, 5-H of phenyl), 7.80 (m, 1 H, 6-H of phenyl), 8.05 (m, 1 H, 4-H of phenyl), 8.24 (m, 1 H, 2-H of phenyl); ms: m/z (%) 228 (100, M^+), 148 (18), 80 (13).

Anal. Calcd. for $C_{13}H_{12}N_2O_2$ (228.25): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.46; H, 5.26; N, 12.17.

Compound **4g** (17%) had mp 85°; ir (potassium bromide): 1625, 1570, 1520 (NO_2), 1475, 1350 (NO_2), 1310, 910 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.72 (s, 3 H, NCH_3), 6.05 (dd, 1 H, 4-H of pyrrole, $J_{4,3}$ = 3.6 Hz, $J_{4,5}$ = 2.7 Hz), 6.54 (dd, 1 H, 3-H of pyrrole, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.8 Hz), 6.84 (dd, 1 H, 5-H of pyrrole, $J_{5,3}$ = 1.8 Hz, $J_{5,4}$ = 2.7 Hz), an AB pattern centered at 6.98 and 7.40 (2 H, HC=CH, J = 16.5 Hz), 7.58 (m, 1 H, 5-H of phenyl), 7.66 (m, 1 H, 6-H of phenyl), 8.00 (m, 1 H, 4-H of phenyl), 8.34 (m, 1 H, 2-H of phenyl); ms: m/z (%) 228 (100, M^+), 148 (12), 80 (10).

Anal. Calcd. for $C_{13}H_{12}N_2O_2$ (228.25): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.34; H, 5.42; N, 12.01.

Photoisomerization Reactions.

A stock solution of each styrylpyrrole (10^{-3} *M*) was prepared and a 10 ml portion of the solution was taken into a 50 ml-round bottomed flask (Pyrex), stoppered, and left at room temperature (25°) under stray light. The solution was examined by gas chromatography or by uv spectroscopy at predetermined time intervals. A 50 ml solution of 10^{-1} *M* was used for reaction with medium pressure mercury lamp.

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