Synthesis of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles

Boris A. Trofimov, Marina V. Markova, Ludmila V. Morozova, and Al′bina I. Mikhaleva

A.E. Favorsky Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, RU-664033 Irkutsk, 1 Favorsky, Russia
E-mail: bat@irioch.irk.ru

Dedicated to academician M. G. Voronkov's 80th birthday
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Abstract
The acid-catalysed dimerization of 1-vinyl-2-alkyl- or 1-vinyl-2,3-dialkylpyrroles proves to be a general approach to the synthesis of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles, a novel family of pyrrole building blocks and intermediates in heterocyclic chemistry.

Keywords: 1-Vinylpyrroles, acid-catalyzed dimerization, 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles

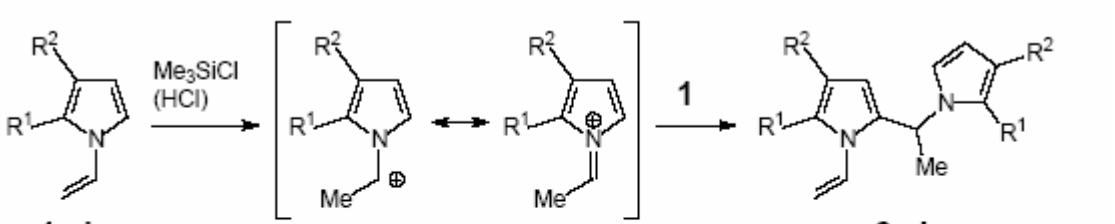
Introduction

Vinylpyrroles are known as structural units of biologically important natural pigments (e.g. hemoglobin, chlorophyll) and valuable intermediates in pyrrole chemistry.[1,2] Among them, the hetaryl-1-vinylpyrroles are less well explored. The only published method of the synthesis of these compounds appears to be still the reaction of hetaryl alkyl ketoximes with acetylene (the Trofimov reaction)[3-5] performed either as a one-pot procedure (with excess acetylene) or with isolation of corresponding 1*H*-pyrroles followed by vinylation. The knowledge about pyrrolyl-1-vinylpyrroles (vinyldipyrroles) relates to the dimerization of 1-vinyl-4,5,6,7-tetrahydroindole.[6-9] Meanwhile, vinyldipyrroles and vinyl(dipyrrolyl)alkanes are of high interest as monomers for conducting cross-linked polypyrrole networks10 as well as versatile building blocks for the pyrrole chemistry and for the design of multidentate ligands.

Results and Discussion

To further contribute in filling this gap, we report on a general approach to the synthesis of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles **2a**–**g** by acid-catalyzed dimerization of substituted 1-

vinylpyrroles **1a**–**g** (Scheme 1).



	a	b	c	d	e	f	g	h
R^1	Me	Me	Me	Me	Et	*n*-Pr	*i*-Bu	Ph
R^2	H	Me	Et	n-Pr	Me	Et	H	H

Scheme 1

The known examples of the transformation of 1-vinylpyrroles (1-vinylpyrrole, 1-vinylindole, 1-vinylcarbazole) in the presence of Brønsted and Lewis acids involve the formation of charge-transfer complexes and subsequent polymerization across the double bond.[11]

In this study, Me_3SiCl and HCl (2%) were used as catalysts for the dimerization of 1-vinylpyrrole, the former reacting as supplier of HCl in the presence of moist reactants.

In early studies, only 1-vinyl-4,5,6,7-tetrahydroindole has been dimerized in the same way with Friedel-Crafts catalysts. Therefore, the applicability of this reaction to other 1-vinylpyrroles remained uncertain. The results reported here show that the reaction is general and adds to synthetic tools of pyrrole chemistry.

As expected, the yield of dimers **2a**–**g** depends on both the reaction conditions and the nature of the pyrrole ring substituents of the starting materials **1a**–**g**. In the presence of Me_3SiCl (2%, 20 °C, 24 h) the dimers **2a,b** and **2d** were formed in 38.9–53.0% yield (Table 1). With HCl the major reaction products were oligomers with the only exception of 1-vinylpyrrole **1e** affording the dimer **2e** in 46.1% yield (Table 1).

Increasing the size of the 3-substituent of the pyrrole **1** (H < Me < *n*-Pr) gave higher yields of dimers **2** (Table 1). Peculiar exceptions are 3-ethyl-2-methyl-1-vinylpyrrole **1c** and 2-(isobutyl)-1-vinylpyrrole **1g**, which did not react and were almost completely recovered from the reaction mixture (95–99%). Attempts to prepare the dimers **2c** and **2g** by increasing the reaction time (up to 48 h) or with higher Me_3SiCl concentration (up to 4%) failed. Low yields (0.8–3.4%) of **2c** and **2g** were obtained only at a reaction temperature at 50 °C or with HCl (Table 1). In 1-vinylpyrrole **1h** the phenyl substituent prevented the dimerization under the above conditions, and only oligomers were formed exclusively.

The 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles **2a**–**g** are colorless or light-yellow liquids that were distilled under reduced pressure; the physico-chemical properties are listed in Table 2.

Table 1. Dimerization of 1-vinylpyrroles **1** at room temperature

R^1	R^2	**1**	Catalyst[a]	Time [h]	**2**	Yield [%]	
						2	Oligomer
Me	H	**a**	Me_3SiCl	24	**a**	38.9	21.4
Me	H	**a**	HCl	24	**a**	17.0	60.0
Me	Me	**b**	Me_3SiCl	24	**b**	48.4	19.0
Me	Me	**b**	HCl[b,c]	24	**b**	20.2	75.3
Me	Et	**c**	Me_3SiCl	24	**c**	Trace	5.0
Me	Et	**c**	Me_3SiCl	48	**c**	Trace	6.3
Me	Et	**c**	Me_3SiCl[c]	48	**c**	Trace	54.2
Me	Et	**c**	Me_3SiCl	16e	**c**	0.8	24.8
Me	Et	**c**	HCl	24	**c**	3.4	62.6
Me	*n*-Pr	**d**	Me_3SiCl	24	**d**	53.0	20.0
Et	Me	**e**	Me_3SiCl	24	**e**	Trace	5.0
Et	Me	**e**	HCl	24	**e**	46.1	17.2
n-Pr	Et	**f**	Me_3SiCl	24	**f**	8.8	7.4
i-Bu	H	**g**	Me_3SiCl[d]	24	**g**	Trace	0.3
i-Bu	H	**g**	Me_3SiCl	16	**g**	Trace	3.8
i-Bu	H	**g**	HCl	24	**g**	2.6	49.2
Ph	H	**h**	Me_3SiCl	24		0	100

[a] Catalyst concentration 2%. [b] Exothermal reaction, up to 70 °C. [c] 36% Aqueous solution. [d] 4% Me_3SiCl. [e] Reaction temperature 50 °C.

Table 2. Physico-chemical properties of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles **2a–f**

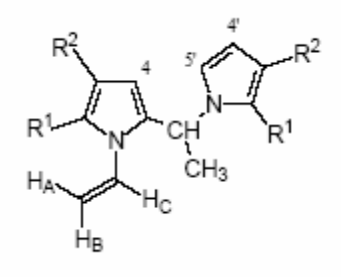
2	bp [°C (mm Hg)]	d_4^{20}	n_D^{20}	Elemental analysis: calcd/found [%]			$M^{+\bullet}$
				C	H	N	
a	112–112.5 (2)	1.0136	1.5440	78.46/78.20	8.47/8.32	13.07/13.26	213
b	123–125 (2)[a]	1.0036	1.5420	79.29/79.12	9.15/9.40	11.56/11.37	241
c	125–126 (0.1)	0.9691	1.5338	79.95/79.98	9.69/9.80	10.36/10.29	269
d	127–128 (0.1)	0.9584	1.5294	80.48/80.62	10.13/9.96	9.39/9.42	297
e	137–140 (2)	0.9790	1.5358	79.95/80.48	9.69/9.70	10.36/10.30	269
f	dec[b]	0.9670	1.5305	80.93/80.58	10.49/10.20	8.58/8.36	-

[a] Crystals upon storage, mp 25.5–28.5 °C. [b] Decomposed during fractionation.

The structure of the dimers **2** was deduced from ^{1}H NMR spectra exhibiting the signals of the CH-CH_3 moiety at δ 5.09–5.17 and 1.60–2.57, respectively, along with those of the pyrrole and

vinyl group signals (Table 3). MS and IR spectra (Tables 2 and 4) are also in agreement with structure **2**. According to the IR study of *N*-vinylpyrroles,[1] all absorptions observed in the IR spectra of **2a**–**h** (Table 4) prove the non-planar conformation of the *N*-vinylpyrrole moiety, lacking any indication of the planar conformation. There is no band at 1590 cm^{-1} assigned to the planar conformation.[1] The band assigned to $\tau_{CH=}$ (960 cm^{-1}) has shifted to higher frequency at 970–980 cm^{-1}, with narrower and less intense appearance; the ω_{CH_2}=-band (860 cm^{-1}) has shifted to 870–880 cm^{-1}, is narrow and reduced in intensity with a shoulder at 850 cm^{-1}. Also the $\omega_{CH=}$-band (585 cm^{-1}) has shifted to 600–630 cm^{-1} with a shoulder at 585 cm^{-1}. The band at 520 cm^{-1} is absent.

Table 3. ^{1}H NMR data of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles **2a**–**h**.



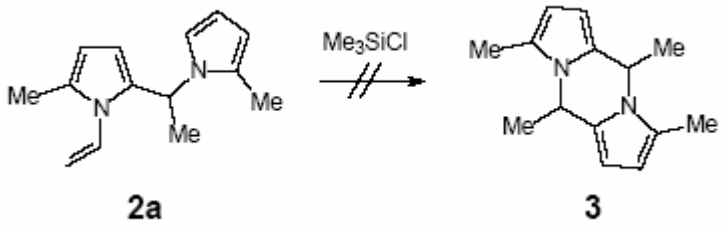
	δH								
2	HA[a]	HB[b]	HC[a,b]	4-H, 4'-H [c]	5'-H[c]	R^1	R^2	CH[d]	CH_3[d]
a	4.96	4.78	6.24	5.95	6.32	CH_3 2.20	H 5.84	5.17	1.62
b	4.89	4.75	6.05	5.84	6.28	CH_3 2.12	CH_3 2.00	5.13	1.60
c	4.89	4.70	6.12	5.88	6.29	CH_3 2.09	CH_3 1.15[d] CH_2 2.41[d]	5.15	1.61
d	4.85	4.66	6.09	5.80	6.25	CH_3 1.60	CH_3 0.87[d] CH_2 0.92[d] CH_2 2.35[d]	5.12	2.57
e	4.80	4.93	6.05	5.80	6.22	CH_3 1.10[d] CH_2 2.55[d]	CH_3 1.64	5.14	2.00
f	4.86	4.45	6.13	5.68	6.89	CH_3 0.95[d] CH_2 1.06[d] CH_2 2.50[d]	CH_3 1.40[d] CH_2 1.55[d]	5.09	1.60
g	5.12	4.60	6.15	5.74	6.97	CH_3 1.10[d] CH 2.43[d] CH_2 1.54[d]	CH_3 5.80	5.14	1.76

[a] J_{AC} = 15.7–16.0 Hz. [b] J_{BC} = 8.9–9.2 Hz; J_{AB} = 0.8 Hz. [c] $J_{4',5'}$ = 2.9–3.2 Hz. [d] J = 6.9–7.1 Hz.

It is conceivable to further cyclize the dipyrrolylethanes **2a–g** in the manner shown in Scheme 2, and the feasibility of this transformation has been checked. The reaction was carried out in very diluted solutions (0.5 g **2a** in 200 mL hexane) at 20 °C in the presence of Me_3SiCl (4.8% and 16%) during 170 h. Cyclization did not occur, the tricyclic diazine derivative **3** was not detected, only the starting material **2a** was recovered (Scheme 2).

Table 4. IR data of 5-[1-(1-pyrrolyl)ethyl]-1-vinylpyrroles **2a–g**

2	ν[m^{-1}] (neat)
a	610 w, 630 w, 708 s, 750, 780, 880, 980 w, 1090, 1150 w, 1220 s, 1280 s, 1370, 1410 s, 1520, 1640, 2840 s, 2900 s, 3100 w
b	610, 630, 710 s, 790, 890, 910, 970, 1020 w, 1040 w, 1060 w, 1110, 1170, 1200, 1310 s, 1350, 1370, 1420, 1490, 1510, 1640, 2860 s, 2910 s, 2970 s, 3090 w
c	630, 690 s, 710 w, 870, 910, 970, 1040 w, 1150, 1210, 1260, 1300 s, 1370, 1420, 1480 s, 1530 w, 1620, 2850, 2910 s, 2950 s, 3090 w
c	620, 690, 708, 870, 890, 910, 970, 1040 w, 1100, 1210, 1250, 1300 s, 1330, 1370, 1420, 1480, 1500 w, 1640, 2860, 2910 s, 2960 s, 3090 w
e	610, 660, 680, 708, 790, 890 w, 970, 1030, 1050, 1100, 1160, 1200, 1250, 1290, 1310 s, 1330 w, 1370, 1420, 1440, 1480, 1500, 1640, 2860 s, 2920 s, 2960 s, 3010, 3090
f	600, 690, 700, 790 w, 870, 930, 970, 1100, 1150 w, 1190, 1200, 1260, 1290, 1320 w, 1370, 1450, 1480, 1630, 2850 s, 2900 s, 2940 w
g	630, 700, 780 w, 820, 880, 970, 1000 w, 1080 w, 1100 w, 1170, 1210, 1280, 1370, 1420, 1460, 1630, 2870, 2930, 2950 s

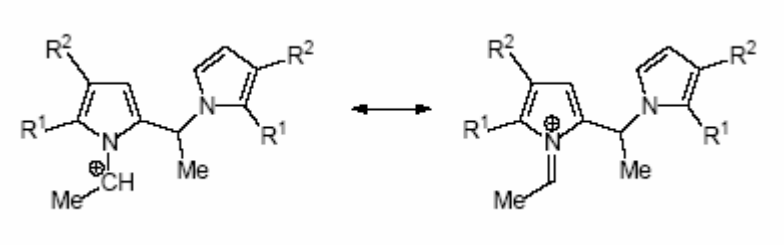


Scheme 2

The reason for this failure cannot be just steric hindrance caused by an unfavorable conformation. Also the reactivity of the *N*-alkyl-pyrrole ring toward intramolecular electrophilic substitution may be decreased considering the strong electron-withdrawing effect of neighboring positively charged pyrrole ring transmitted through the sp^3 carbon atom by inductive (non-conjugative) effect as well as by a "through-space" polarization of the neighboring uncharged pyrrole ring (Scheme 3).

The decreased reactivity of the *N*-vinyl group of **2a**–**h** is also manifests by the fact that

dimers **2** cannot add phenols in the presence of CF_3COOH, whereas the corresponding monomers **1** form the corresponding 1-(1-aryloxyethyl)pyrroles in up to 60% yields.[12] This may be caused also by the lack of conjugation between the *N*-vinyl and the pyrrole moieties due to their noncoplanarity. This seems to be supported by the above mentioned changes in the IR spectra,[9] and by ^{1}H NMR evidence. The proton signals of the vinyl CH_2 group are shifted downfield by 0.4 ppm relative to the signals in pyrroles **1a**–**h** (Table 3). As has been shown for the dimer of 1-vinyl-4,5,6,7-tetrahydroindole[9] (with the ^{13}C signal of the vinyl β-C shifted downfield by 10.4–11 ppm), this is the largest downfield shift known for these nuclei in the 1-vinylpyrroles series; correspondingly, this reflects the strongest deviation from coplanarity and conjugation.



Scheme 3

Experimental Section

General Procedures. Spectra (films) were run on a Specord IR-75 spectrometer; ^{1}H NMR spectra of $CDCl_3$ solutions with TMS as an internal standard were recorded on a Tesla BS-567 instrument (100 MHz). Mass spectra were run on an LKB 2091 CMC-MS spectrometer, ioniziation energy 60 eV, SE-30 phase, ion source temperature 250 °C.

2-Methyl-5-[1-(2-methyl-3-propyl-1*H*-pyrrol-1-yl)ethyl]-3-propyl-1-vinyl-1*H*-pyrrole (2d). Typical procedure. To 2-methyl-3-propyl-1-vinyl-1*H*-pyrrole (**1d**) (3.00 g, 20.1 mmol) was added with stirring chloro(trimethyl)silane (0.06 g, 0.5 mmol), and the reaction mixture was allowed to stand at room temperature for 24 h. The resultant dark-red resin was extracted with diethyl ether (3 × 30 mL), and 0.1 M KOH in ethanol (0.02 mL) was added to the extract for binding the catalyst. The extract was washed with water (4 × 100 mL) until neutral reaction and dried with K_2CO_3. The ether was stripped off, and the reaction mixture was distilled in vacuum to give **2d** (1.59 g, 53%). The distillation residue (a dark-brown resin of oligomer) was dried until constant weight (0.6 g, 20%).

The dimerization of other 1-vinylpyrroles **1** was analogous (Table 1). Dimers 3-ethyl-5-[1-(3-ethyl-2-propyl-1*H*-pyrrol-1-yl)ethyl]-2-propyl-1-vinyl-1*H*-pyrrole (**2f**) and 2-isobutyl-5-[1-(2-isobutyl-1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrrole (**2g**) were isolated by column chromatography

on aluminum oxide with hexane as eluent. Experimental and spectral data of 5-[1-(1*H*-pyrrol-1-yl)ethyl]-1-vinyl-1*H*-pyrroles **2a**–**f** are listed in Tables 2–4. Due to the low yield of dimer **2g** the structure was determined by the ^{1}H NMR spectrum only (Table 3).

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