An Efficient Route to 1-Vinylpyrrole-2-carbaldehydes

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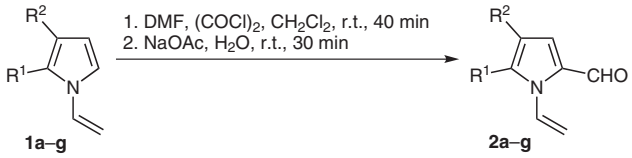
Abstract: 1-Vinylpyrroles are formylated by the *N*,*N*-dimethylformamide/oxalyl chloride reagent system (CH_2Cl_2, r.t., 40 min) to give the corresponding 1-vinylpyrrole-2-carbaldehydes in yields up to 97%.

Key words: aldehydes, pyrroles, formylation, oxalyl chloride, Vilsmeier–Haack reaction

Pyrroles bearing functional groups have been finding ever-increasing application in the synthesis of pharmaceuticals and analogues of natural compounds.[1] New antibiotics, pheromones, toxins, inhibitors of cell division and immunomodulating agents containing the pyrrole core have been discovered.[2] Pyrrole-2-carbaldehydes have been used as intermediates in the synthesis of diverse oligopyrrole systems,[3] anion receptors in biomedical analysis,[4] porphyrins,[5] models for the investigation of multiple sclerosis[6] and expansion of the genetic alphabet,[7] ligands for metallocomplexes,[8] and conjugated polymers.[9] Pyrrole-2-carbaldehydes are also used in the modification of natural structures such as proteins[10] and lipids.[11] Chemical transformation of pyrrole-2-carbaldehydes has allowed valuable compounds such as carbolines,[12] cyanopyrroles,[13] and divinylpyrroles[14] to be obtained. The synthetic potential of the aldehyde moiety combined with the biological importance of pyrroles has attracted the continuous attention of chemists all over the world to this class of compounds.

In the last years, 1-vinylpyrroles, readily available in one step from ketoximes and acetylenes by the Trofimov reaction,[15] have been efficiently applied in the synthesis of functionalized pyrroles. Recently, we[16] have developed a general method for the synthesis of the previously unknown 1-vinylpyrrole-2-carbaldehydes **2**, based on the Vilsmeier–Haack reaction modified for 1-vinylpyrroles **1**. A modification was required because of the sensitivity of the *N*-vinyl group towards electrophilic attack from the *N*,*N*-dimethylformamide/phosphoryl chloride reagent that reduced the chemoselectivity of the reaction. As a result, 1-vinylpyrrole-2-carbaldehydes containing aryl and hetaryl substituents, including fused polycyclic systems, e.g. 1-vinyl-4,5-dihydrobenz[*g*]indole-2-carbaldehyde (**2d**), were obtained in good yields (Table 1, entry 4), since such substituents decrease the sensitivity of the vinyl group towards electrophilic reagents. However, in the case of 1-vinylpyrroles containing donor (alkyl) substituents, the yields of the target aldehydes were significantly reduced. For instance, from 1-vinyl-4,5,6,7-tetrahydroindole (**1b**) the corresponding formyl derivative **2b** was obtained in only 56% yield (Table 1, entry 2),[16] and the formylation of 3-ethyl-2-propyl-1-vinylpyrrole (**1a**) gave **2a** in 28% yield only (entry 1). To increase the efficiency of this approach in a series of 1-vinyl-2-alkyl- and 1-vinyl-2,3-dialkylpyrroles, we have tried to replace the *N*,*N*-dimethylformamide/phosphoryl chloride system by a milder formylating agent.



Scheme 1

It is known that the formylation of pyrroles, in particular dipyrromethanes sensitive to the action of acidic reagents, sometimes requires the use of an *N*,*N*-dimethylformamide/benzoyl chloride system instead of the classic Vilsmeier reagent.[17] However, our experiments have shown that 1-vinylpyrroles are not formylated by the *N*,*N*-dimethylformamide/benzoyl chloride reagent under the conditions reported earlier for this class of compounds[16] (–78 °C, 3 h): the conversion of 1-vinyl-4,5-dihydrobenz[*g*]indole (**1d**) into the corresponding formyl derivative **2d** was only 3.5% (GLC analysis). At a higher reaction temperature (0 °C), the conversion of 1-vinylpyrrole **1d** to aldehyde **2d** increased to 11.7%, while under reflux (DCE, 57 °C, 3 h) of the same reactants the conversion of pyrrole **1d** did not exceed 33%. The *N*,*N*-dimethylformamide/benzoyl chloride complex appears to be unsuitable for introduction of the formyl group to 1-vinylpyrroles.

The use of oxalyl chloride (among a number of other formylating reagents) in the Vilsmeier–Haack reaction was briefly mentioned in only a few papers[18] and patents.[19] In one of these papers, the influence of the substituent in an amide component was studied,[18c] showing that the chloro anhydride structure had 'only a very small effect' on the reaction results. Oxalyl chloride was used in-

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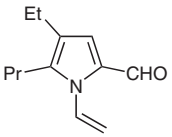
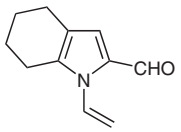
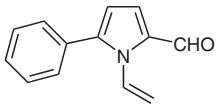
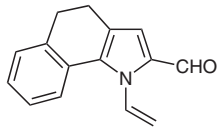
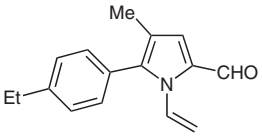
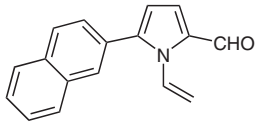
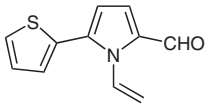
Table 1 Comparison of the *N*,*N*-Dimethylformamide/Phosphoryl Chloride and *N*,*N*-Dimethylformamide/Oxalyl Chloride Reagent Systems in the Formylation of 1-Vinylpyrroles

Entry	Product		Isolated yield[a] (%)	
			DMF/ $POCl_3$	DMF/ $(COCl)_2$
1		**2a**	28[b]	48
2		**2b**	56[16]	72
3		**2c**	66[16]	93
4		**2d**	91[16]	89
5		**2e**	–[b]	83
6		**2f**	72[20]	81
7		**2g**	88[16]	97

[a] The products were identified by IR and ^1H and ^{13}C NMR spectroscopy and elemental analysis.
[b] Previously unknown.

stead of phosphorus oxychloride[18a] to afford an iminium salt (the precursor of pyrrole-2-carbaldehydes), since the formation of phosphorus-containing side products was thus avoided. However, no evidence that oxalyl chloride was a 'softer' reagent was presented.

Here we report that the replacement of phosphoryl chloride by oxalyl chloride in the formylation of 1-vinylpyrroles **1** makes it possible to increase the yields of 1-vinylpyrrole-2-carbaldehydes **2** to almost quantitative with complete conversion of the starting 1-vinylpyrroles **1**; it also makes it possible to perform all stages of the reaction at room temperature (instead of at –78 °C, as the former protocol[16] required) (Scheme 1, Table 1). Stirring of the reaction mixture in dichloromethane for 40 minutes resulted in full consumption of the starting 1-vinylpyrroles **1** (GLC analysis).

This method was successfully applied to various 1-vinylpyrroles **1** containing aliphatic, aromatic, condensed aromatic, and heteroaromatic substituents, as well as to 1-vinylpyrroles condensed with cycloaliphatic and dihydronaphthalene systems (see Table 1). As shown in Table 1, the yields of 1-vinylpyrrole-2-carbaldehydes **2a**,**b** containing donor (alkyl) substituents were increased approximately by 20% (entries 1 and 2). Moreover, the yields of 1-vinylpyrroles with aryl and hetaryl substituents **2c**,**e**–**g** were also increased (by 9–27%) (entries 3 and 5–7).

It may be concluded that, in general, oxalyl chloride provides the best results in the formylation of 1-vinylpyrroles, being a less aggressive reagent than phosphoryl chloride, more active than benzoyl chloride, and safer and more convenient to handle than other formylating reagents.[21]

The reaction proceeds at room temperature (instead of –78 °C[16]) and needs a shorter time (40 min instead of 3 h[16]). The use of the new method of 1-vinylpyrrole formylation by the *N*,*N*-dimethylformamide/oxalyl chloride reagent apparently suppresses oligomerization side reactions and the removal of *N*-vinyl groups that occurs in the case of the *N*,*N*-dimethylformamide/phosphoryl chloride reagent.

Melting points were measured on a Kofler micro hot stage apparatus. IR spectra were measured on a Bruker IFS-25 as KBr pellets or films. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX spectrometer. Oxalyl chloride, DMF and benzoyl chloride are commercial products. The 1-vinylpyrroles were prepared according to a published procedure.[15a]

1-Vinylpyrrole-2-carbaldehydes 2; General Procedure

$(COCl)_2$ (1.40 g, 11.0 mmol) was added dropwise (2–3 min) to DMF (0.80 g, 11.0 mmol) at ~10 °C (cold H_2O), and the white crystals obtained were stirred for 15 min without cooling. Then CH_2Cl_2 (10.0 mL) was added, and a soln of 1-vinylpyrrole **1** (10 mmol) in CH_2Cl_2 (15.0 mL) was added dropwise over 10 min at 25 °C. The resulting mixture was stirred for 0.5 h at r.t. Then a soln of NaOAc (4.10 g, 50 mmol) in H_2O (45 mL) was added and the stirring was continued for 0.5 h at r.t. The lower (organic) layer was separated. The aqueous layer was extracted with Et_2O (5 × 30 mL). The combined organic phases were washed with sat. aq $NaHCO_3$ (3 × 30 mL) and H_2O (3 × 30 mL), and dried (K_2CO_3). The residue obtained after evaporation of the Et_2O was purified on basic alumina (hexane–Et_2O, 2:1); this gave formylpyrrole **2**.

4-Ethyl-5-propyl-1-vinylpyrrole-2-carbaldehyde (2a)

From 1-vinylpyrrole **1a** (1.63 g, 10 mmol), **2a** was obtained.

Yield: 0.92 g (48%); yellow oily liquid.

IR (film, KBr): 3111, 3049, 2943, 2933, 2867, 2862, 2809, 2727, 1670, 1641, 1580, 1475, 1418, 1375, 1318, 1285, 1250, 1212, 1150, 1125, 1075, 1030, 969, 915, 880, 855, 800, 775, 745, 710, 684, 596, 515, 487 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.43 (s, 1 H, CHO), 7.19 (dd, $^3J_{B-X}$ = 15.8 Hz, $^3J_{A-X}$ = 8.7 Hz, 1 H, H_X), 6.84 (s, 1 H, H-3), 5.26 (d, $^3J_{A-X}$ = 8.7 Hz, 1 H, H_A), 5.21 (d, $^3J_{B-X}$ = 15.8 Hz, 1 H, H_B), 2.61 [m, 2 H, CH_2 (Pr)], 2.41 [q, ^3J = 7.5 Hz, 2 H, CH_2 (Et)], 1.53 [m, 2 H, CH_2 (Pr)], 1.17 [t, ^3J = 7.5 Hz (Et), 3 H, CH_3], 0.93 [t, ^3J = 7.3 Hz, 3 H, CH_3 (Pr)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.2 (C=O), 140.3 (C-5), 131.6 ($C_α$), 131.2 (C-2), 126.4 (C-4), 123.3 (C-3), 111.3 ($C_β$), 26.6 [CH_2 (Pr)], 22.5 [CH_2 (Pr)], 18.9 [CH_2 (Et)], 15.0 [CH_3 (Et)], 14.0 [CH_3 (Pr)].

Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.39; H, 8.91; N, 7.40.

4,5,6,7-Tetrahydro-1-vinylindole-2-carbaldehyde (2b)
From 1-vinylpyrrole **1b** (1.47 g, 10 mmol), **2b** was obtained.

Yield: 1.26 g (72%); yellowish oil.

IR (film, KBr): 3120, 3085, 2933, 2850, 2786, 2715, 1658, 1641, 1569, 1477, 1460, 1440, 1424, 1387, 1323, 1288, 1255, 1236, 1212, 1157, 1133, 1110, 1087, 1060, 966, 945, 869, 831, 815, 747, 705, 686, 636, 550, 489 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.40 (s, 1 H, CHO), 7.54 (dd, $^3J_{A–X}$ = 9.1 Hz, $^3J_{B–X}$ = 16.1 Hz, 1 H, H_X), 6.70 (s, 1 H, H-3), 5.05 (d, $^3J_{B–X}$ = 16.1 Hz, 1 H, H_B), 5.03 (d, $^3J_{A–X}$ = 9.1 Hz, 1 H, H_A), 2.67 (t, $^3J_{6–7}$ = 6.0 Hz, 2 H, H-7), 2.51 (t, $^3J_{4–5}$ = 6.0 Hz, 2 H, H-4), 1.78 (m, 2 H, H-6), 1.72 (m, 2 H, H-5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0 (C=O), 139.8 (C-2), 131.3 ($C_α$), 131.1 (C-7a), 124.5 (C-3), 122.2 (C-3a), 106.4 ($C_β$), 24.3 (C-4), 23.2 (C-7), 22.7 (C-5, C-6).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.34; H, 7.53; N, 8.01.

5-Phenyl-1-vinylpyrrole-2-carbaldehyde (2c)
From 1-vinylpyrrole **1c** (1.69 g, 10 mmol), **2c** was obtained.

Yield: 1.83 g (93%); yellowish oil.

IR (film, KBr): 3121, 3055, 3020, 2987, 2929, 2800, 2727, 1655, 1630, 1593, 1559, 1533, 1492, 1450, 1440, 1428, 1401 1359, 1324, 1285, 1222, 1059, 1032, 951, 919, 888, 865, 830, 746, 680, 660, 606, 537, 462 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.62 (s, 1 H, CHO), 7.40 (m, 5 H, Ph), 7.35 (dd, $^3J_{B–X}$ = 15.8 Hz, $^3J_{A–X}$ = 8.7 Hz, 1 H, H_X), 7.05 (d, $^3J_{3–4}$ = 3.9 Hz, 1 H, H-3), 6.35 (d, $^3J_{3–4}$ = 3.9 Hz, 1 H, H-4), 5.08 (d, $^3J_{A–X}$ = 8.7 Hz, 1 H, H_A), 4.87 (d, $^3J_{B–X}$ = 15.8 Hz, 1 H, H_B).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.0 (C=O), 142.4 (C-2), 133.3 (C_i), 131.0 (C-5), 131.4 (C_p), 130.1 (C_m), 128.1 (C_o), 128.3 (C-3), 124.4 (C-4), 112.6 ($C_α$), 112.4 ($C_β$).

Anal. Calcd for $C_{13}H_{11}NO$: C, 79.17; H, 5.62; N, 7.10. Found: C, 79.08; H, 5.57; N, 7.21.

1-Vinyl-4,5-dihydrobenzo[*g*]indole-2-carbaldehyde (2d)
From 1-vinylpyrrole **1d** (1.95 g, 10 mmol), **2d** was obtained.

Yield: 1.99 g (89%); beige crystals; mp 136–138 °C (Lit.[16] 133–135 °C).

IR (KBr): 3095, 3020, 2987, 2957, 2899, 2841, 1643, 1616, 1533, 1511, 1462, 1438, 1417, 1370, 1335, 1289, 1236, 1180, 1155, 1136, 1097, 1044, 1029, 948, 921, 915, 877, 842, 777, 765, 738, 710, 685, 666, 637, 600, 575, 539, 524, 477, 436 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.59 (s, 1 H, CHO), 7.75 (d, $^3J_{6–7}$ = 8.1 Hz, 1 H, H-6), 7.49 (dd, $^3J_{B–X}$ = 15.7 Hz, $^3J_{A–X}$ = 8.3 Hz, 1 H, H_X), 7.27 (d, $^3J_{8–9}$ = 9.1 Hz, 1 H, H-9), 7.20 (m, 2 H, H-7, H-8), 6.91 (s, 1 H, H-3), 5.41 (d, $^3J_{A–X}$ = 8.3 Hz, 1 H, H_A), 5.38 (d, $^3J_{B–X}$ = 15.7 Hz, 1 H, H_B), 2.91 (t, $^3J_{4–5}$ = 7.2 Hz, 2 H, H-4), 2.69 (t, $^3J_{4–5}$ = 7.2 Hz, 2 H, H-5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.1 (C=O), 138.7 (C-5a), 136.1 (C-9b), 133.8 (C-2), 132.1 ($C_α$), 128.2 (C-7), 128.0 (C-9a), 127.5 (C-6), 126.5 (C-8), 125.4 (C-3a), 124.2 (C-9), 121.1 (C-3), 113.9 ($C_β$), 30.5 (C_5), 22.2 (C-4).

Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.74; H, 5.94; N 6.09.

5-(4-Ethylphenyl)-4-methyl-1-vinylpyrrole-2-carbaldehyde (2e)
From 1-vinylpyrrole **1e** (2.11 g, 10 mmol), **2e** was obtained.

Yield: 1.98 g (83%); red viscous oil.

IR (film, KBr): 3099, 3062, 3039, 2932, 2888, 2840, 1637, 1538, 1508, 1463, 1419, 1372, 1331, 1294, 1193, 1165, 1128, 1092, 1029, 976, 918, 876, 835, 763, 724, 669, 634, 606, 469, 432 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.69 (s, 1 H, CHO), 7.43 (dd, $^3J_{B–X}$ = 15.8 Hz, $^3J_{A–X}$ = 8.8 Hz, 1 H, H_X), 7.38 (m, 2 H, H_m), 7.33 (m, 2 H, H_o), 7.03 (s, 1 H, H-4), 5.04 (d, $^3J_{A–X}$ = 8.8 Hz, 1 H, H_A), 4.85 (d, $^3J_{B–X}$ = 15.8 Hz, 1 H, H_B), 2.82 (q, ^3J = 7.6 Hz, 2 H, CH_2), 2.14 (s, 3 H, CH_3), 1.40 (t, ^3J = 7.6 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.8 (C=O), 143.6 (C_p), 139.9 (C-5), 132.2 (C-2), 131.4 ($C_β$), 130.9 (C_o), 130.1 (C_i), 127.8 (C_m), 123.9 (C-3), 120.2 (C-4), 110.6 ($C_α$), 28.7 (CH_2, Et), 15.5 (CH_3, Et), 12.2 (CH_3, Me).

Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.42; H, 7.25; N, 5.93.

5-(2-Naphthyl)-1-vinylpyrrole-2-carbaldehyde (2f)
From 1-vinylpyrrole **1f** (2.19 g, 10 mmol), **2f** was obtained.

Yield: 2.00 g (81%); crimson oily liquid.

IR (film, KBr): 3290, 3121, 3059, 2959, 2921, 2835, 2800, 2788, 2725, 1661, 1604, 1539, 1488, 1447, 1424, 1366, 1323, 1317, 1294, 1277, 1250, 1218, 1133, 1096, 1040, 955, 898, 864, 838, 825, 787, 767, 752, 696, 677, 666, 632, 478 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.71 (s, 1 H, CHO), 7.99 (s, 1 H, H_{Ar}), 7.87 (m, 3 H, H_{Ar}), 7.55 (m, 3 H, H_{Ar}), 7.49 (dd, $^3J_{B–X}$ = 15.7 Hz, $^3J_{A–X}$ = 8.6 Hz, 1 H, H_X), 7.17 (d, 1 H, J = 4.1 Hz, H-3), 6.55 (d, 1 H, J = 4.1 Hz, H-4), 5.11 (d, $^3J_{A–X}$ = 8.6 Hz, 1 H, H_A), 4.90 (d, $^3J_{B–X}$ = 15.7 Hz, 1 H, H_B,).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5 (C=O), 142.5 (C-5), 133.3 (C-2), 133.2 (C_{Ar}), 132.8 (C_{Ar}), 131.5 ($C_α$), 129.0–126.7 (8C, C_{Ar}) 124.6 (C-3), 113.3 (C-4), 112.9 ($C_β$).

Anal. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.65; H, 5.43; N, 5.55.

5-(2-Thienyl)-1-vinylpyrrole-2-carbaldehyde (2g)
From 1-vinylpyrrole **1g** (1.75 g, 10 mmol), **2g** was obtained.

Yield: 1.97 g (97%); cherry-colored crystals; mp 35–37 °C (Lit.[16] 34–35 °C).

IR (KBr): 3100, 3076, 2992, 2841, 2819, 2794, 2727, 1669, 1655, 1640, 1592, 1563, 1511, 1470, 1435, 1415, 1361, 1330, 1313, 1292, 1233, 1199, 1111 1094, 1076, 1038, 1011, 958, 906, 851, 704, 677, 634, 616, 581, 511, 464 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.65 (s, 1 H, CHO), 7.41 (dd, $^3J_{3′–4′}$ = 3.6 Hz, $^3J_{3′–5′}$ = 1.1 Hz, 1 H, H-3′), 7.30 (dd, $^3J_{B–X}$ = 15.7 Hz, $^3J_{A–X}$ = 8.4 Hz, 1 H, H_X), 7.22 (dd, $^3J_{3′–4′}$ = 3.6 Hz, $^3J_{4′–5′}$ = 5.1 Hz, 1 H, H-4′), 7.11 (dd, $^3J_{4′–5′}$ = 5.1 Hz, $^3J_{3′–5′}$ = 1.1 Hz, 1 H, H-5′), 7.00 (d, $^3J_{3–4}$ = 4.0 Hz, 1 H, H-3), 6.54 (d, $^3J_{3–4}$ = 4.0 Hz, 1 H, H-4), 5.39 (d, $^3J_{A–X}$ = 8.4 Hz, 1 H, H_A), 5.17 (d, $^3J_{B–X}$ = 15.7 Hz, 1 H, H_B).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3 (C=O), 135.3 (C-2′), 133.7 (C-2), 132.3 (C-5), 130.6 ($C_α$), 128.1 (C-5′), 127.7 (C-4′), 127.0 (C-3′), 123.4 (C-3), 114.4 ($C_β$), 112.9 (C-4).

Anal. Calcd for $C_{11}H_9NOS$: C, 65.00; H, 4.46; N, 6.89; S, 15.77. Found: C, 65.10; H, 4.38; N, 6.98; S, 15.81.

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References

(1) Brandsma, L. *Eur. J. Org. Chem.* **2001**, 4569.
(2) (a) Mikhaleva, A. I.; Schmidt, E. Yu. In *Selected Methods for Synthesis and Modification of Heterocycles*; Kartsev, V. G., Ed.; IBS Press: Moscow, **2002**, 331. (b) Romila, D.; Schlingmann, G.; Valerie, S.; Xidong, F.; Carter, G. *J. Nat. Prod.* **2005**, *68*, 277.
(3) (a) Hue, T.; Scott, A. I. *Tetrahedron Lett.* **1998**, *39*, 6651. (b) Sessler, J. L.; Roznyatovskiy, V.; Pantos, J. D.; Borisova, N. E.; Reshetova, M. D.; Lynch, V. M.; Krustalev, V. N.; Ustynyuk, J. A. *Org. Lett.* **2005**, *7*, 5277.
(4) Hunt, J. T.; Mitt, T.; Borzilleri, R.; Gullo-Brown, J.; Fargnolli, J.; Fink, B.; Han, W. C.; Mortillo, S.; Vite, G.; Wautlet, B.; Wong, T.; Yu, C.; Zheng, X.; Bhide, R. *J. Med. Chem.* **2004**, *47*, 4054.
(5) (a) Furuta, H.; Maeda, H.; Furuta, T.; Osuka, A. *Org. Lett.* **2000**, *2*, 187. (b) Wiehe, A.; Ruppa, C.; Senge, M. O. *Org. Lett.* **2002**, *4*, 3807.
(6) Bouérat, L.; Fensholdt, J.; Liang, X.; Havez, S.; Nielsen, S. F.; Hansen, J. R.; Bolvig, S.; Andersson, C. *J. Med. Chem.* **2005**, *48*, 5412.
(7) Mutsui, T.; Kitamura, A.; Kimora, M.; To, T.; Sato, A.; Hirao, I.; Yokoyama, S. *J. Am. Chem. Soc.* **2003**, *125*, 5298.
(8) Westmoreland, I. *Synthetic Page* **2005**, 224; see http://www.syntheticpages.org/pages/224.
(9) (a) Simionescu, C. I.; Grigoras, M.; Cianga, I.; Diaconu, I.; Farcas, A. *Polym. Bull.* **1994**, *32*, 257. (b) Simionescu, C. I.; Grovu-Ivanoiu, M.; Grigoras, M.; Cianga, I. *Angew. Makromol. Chem.* **1994**, *221*, 103.
(10) (a) Nagaraj, R. H.; Monnier, V. M. *Biochim. Biophys. Acta* **1995**, *1253*, 75. (b) Hofmann, T. *J. Agric. Food Chem.* **1998**, *46*, 3902.
(11) Utzman, C. M.; Lederer, M. O. *Carbohydr. Res.* **2000**, *325*, 157.
(12) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 7048.
(13) Pavlov, P. A. *Russ. J. Org. Chem.* **2001**, *37*, 1310.
(14) Settambolo, R.; Marani, M.; Caiazzo, A. *J. Org. Chem.* **1998**, *63*, 10022.
(15) (a) Trofimov, B. A.; Mikhaleva, A. I. *N-Vinylpyrroles*; Nauka: Novosibirsk, **1984**, 264; in Russian. (b) Bean, G. P. In *The Chemistry of Heterocyclic Compounds. Pyrroles*, Part 2; Jones, R. A., Ed.; Wiley Interscience: New York, **1992**, 105. (c) Trofimov, B. A. In *Pyrroles*, Part 1; Jones, R. A., Ed.; Wiley: New York, **1992**, 131. (d) Abele, E.; Lukevics, E. *Heterocycles* **2000**, *53*, 2285. (e) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2491.
(16) Mikhaleva, A. I.; Zaitsev, A. B.; Ivanov, A. V.; Schmidt, E. Yu.; Vasil'tsov, A. M.; Trofimov, B. A. *Tetrahedron Lett.* **2006**, *47*, 3693.
(17) (a) Vatsuro, K. V.; Mishchenko, G. L. *Named Reactions in Organic Chemistry*; Khimiya: Moscow, **1976**, 115; in Russian. (b) Beer, P. D.; Cheetham, A. G.; Drew, M. G. B.; Fox, O. D.; Hayes, E. J.; Rolls, T. D. *Dalton Trans.* **2003**, 603.
(18) (a) Barnett, G. H.; Anderson, H. J.; Loader, C. E. *Can. J. Chem.* **1980**, *58*, 409. (b) Faber, K.; Anderson, H. J.; Loader, C. E.; Daley, A. S. *Can. J. Chem.* **1984**, *62*, 1046. (c) Meth-Cohn, O.; Ashton, M. *Tetrahedron Lett.* **2000**, *41*, 2749.
(19) (a) Zoller, G.; Beyerle, R.; Schindler, U. U.S. Pat. 4,966,901, **1990**; *Chem. Abstr.* **1990**, *113*, 6150x. (b) Zoller, G.; Beyerle, R.; Schindler, U. US Patent 5043348, **1991**; *Chem. Abstr.* **1989**, *110*, 135078. (c) Liebeskind, L. S.; Wansheng, L. US Patent 6441194 B1, **2002**; *Chem. Abstr.* **2002**, *134*, 311103.
(20) Mikhaleva, A. I.; Ivanov, A. V.; Vasil'tsov, A. M.; Ushakov, I. A.; Ma, J. S.; Yang, G. *Khim. Geterotsikl. Soedin.* **2008**, 1384.
(21) Kantlehner, W. *Eur. J. Org. Chem.* **2003**, 2530; and references cited therein.