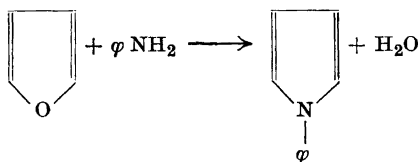


The Preparation of Pyrroles from Furans

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Yur'ev et al. have described a method for transforming a furan into the corresponding pyrrole or N-substituted pyrrole¹⁻⁷. The furan and a large excess of ammonia or an amine were passed, in the vapor phase, over aluminum oxide at about 400°, whereby the pyrrole and water were formed. In this way Yur'ev prepared 14 pyrroles in moderate yields (3-41 per cent). Thus furan and aniline gave a 24 per cent yield of 1-phenylpyrrole.



Another route from furans to pyrroles has recently been reported⁸. 2-(Acetamidomethyl)-furan (I) was methoxylated to 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran II, this compound was hydrogenated catalytically to 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran III, which with aniline in acetic acid gave 1-phenyl-2-(acetamidomethyl)-pyrrole IV. The overall yield of this 3-step reaction was 81 per cent.

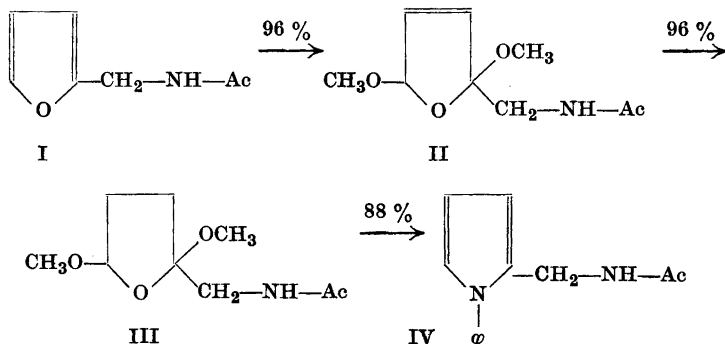


Table 1. Pyrrole compounds from furans. New compounds are marked with an asterisk.

Furan compound	RNH ₂ compound	Pyrrole compound	Yields (%) based upon the furan compound	
			Yur'ev's method (one step)	Our method (three steps)
Furan	Ammonia	Pyrrole	30 ¹	40
—	Methylamine	1-Methylpyrrole	25 ⁶	
—	Ethylamine	1-Ethylpyrrole	27 ⁶	
—	<i>n</i> -Butylamine	1- <i>n</i> -Butylpyrrole		21
—	<i>n</i> -Amylamine	1- <i>n</i> -Amylpyrrole	14 ²	28
—	Aniline	1-Phenylpyrrole	24 ³	59
—	<i>o</i> -Toluidine	1- <i>o</i> -Tolylpyrrole	41 ³	54
—	<i>p</i> -Toluidine	1- <i>p</i> -Tolylpyrrole	21 ³	
—	Benzylamine	1-Benzylpyrrole	3 ⁷	
—	<i>p</i> -Phenylene-diamine	1,1'- <i>p</i> -Phenylene-dipyrryl *		31
2-Methylfuran	Ammonia	2-Methylpyrrole	24 ⁴	25
—	Aniline	1-Phenyl-2-methylpyrrole	12 ⁵	51
—	<i>o</i> -Toluidine	1- <i>o</i> -Tolyl-2-methylpyrrole	10 ⁵	
—	<i>p</i> -Toluidine	1- <i>p</i> -Tolyl-2-methylpyrrole	10 ⁵	
2-(Acetamidomethyl)-furan	<i>n</i> -Amylamine	1- <i>n</i> -Amyl-2-(acetamidomethyl)-pyrrole*		69
Furfuryl methyl ether	Aniline	1-Phenyl-2-(methoxymethyl)-pyrrole *		17
Furfural dimethyl acetal	Ammonia	2-Pyrrolecarboxaldehyde		24
—	Aniline	1-Phenyl-2-pyrrolecarboxaldehyde *		35
Methyl 2-furoate	Ammonia	Methyl 2-pyrrolecarboxylate		11
—	Aniline	Methyl 1-phenyl-2-pyrrolecarboxylate		36
2,5-Dimethylfuran	Ammonia	2,5-Dimethylpyrrole	16 ⁷	
2-Ethylfuran	Ammonia	2-Ethylpyrrole	5 ²	
3-Isopropylfuran	Aniline	1-Phenyl-3-isopropylpyrrole *		35

The transformation of furans into pyrroles by way of the 2,5-dimethoxy-tetrahydrofurans has now been used for the preparation of 15 pyrroles. The final step, the reaction between the tetrahydrofuran and ammonia or an amine, was usually carried out in acetic acid as mentioned above, but some pyrroles were also prepared in the liquid phase without a solvent, or in the vapor phase over aluminum oxide. Our results, together with those of Yur'ev, are summarized in Table 1. Five of the pyrroles prepared by us are new compounds.

The methoxylation of furfural dimethyl acetal has been described previously⁹, but the structure of the resulting dimethoxy compound was not determined. Since dimethoxytetrahydrofurfural dimethyl acetal now has been transformed into 2-pyrrolecarboxaldehyde and 1-phenyl-2-pyrrole-carboxaldehyde, the methoxy groups must be in the 2,5-positions.

It will be seen from the above that the new method, apart from the preparation of pyrroles, may also be used to prove the structure of new dimethoxy-dihydro- and dimethoxytetrahydrofurans.

EXPERIMENTAL

Microanalyses by E. Boss and K. Glens

Materials. a) *2,5-Dimethoxytetrahydrosilvan.* 30.0 g of dimethoxydihydrosilvan⁹ and 100 ml of methanol (technical product) were shaken with 1.0 g of Raney nickel under 100 atmospheres of hydrogen for 1 hour. The hydrogenation product was isolated by distillation through a short packed column. Yield 24.5 g of dimethoxytetrahydrosilvan = 81 %; colourless liquid, b.p.₇₅₉ = 147–155°; $n_D^{25} = 1.4166$.

$C_5H_8O(OCH_3)_2$ (146.2) Calc. C 57.5 H 9.7 OCH_3 42.5
Found » 57.5 » 9.5 » 42.8

b) *2,5-Dimethoxy-3-isopropyltetrahydrofuran.* 3.00 g of 2,5-dimethoxy-3-isopropyl-2,5-dihydrofuran¹⁰ and 15 ml of anhydrous methanol were shaken with 0.2 g of Raney nickel under 100–110 atmospheres at 70–90° for 3.5 hours. Yield 1.68 g of dimethoxyisopropyltetrahydrofuran = 56 %; colourless liquid, b.p.₁₄ = 74–76°; $n_D^{25} = 1.4240$.

$C_7H_{12}O(OCH_3)_2$ (174.2) Calc. C 62.0 H 10.4 OCH_3 35.6
Found » 62.0 » 10.4 » 34.5

c) *2,5-Dimethoxytetrahydrofurfural, dimethyl acetal.* 17.4 g of dimethoxydihydrofurfural dimethyl acetal⁹ and 35 ml of anhydrous methanol were shaken with 2.0 g of Raney nickel under 100 atmospheres for 4 hours. The product was isolated by distillation.

Fraction (g)	B.p. ₁₀	n_D^{25}
1 (6.1)	95°	1.4327
2 (6.8)	95–96°	1.4328
3 (3.2)	96–102°	1.4331

Yield (all fractions) 16.1 g of dimethoxytetrahydrofurfural dimethyl acetal = 92 % (colourless liquid). Fraction 2 was analyzed.

$C_5H_6O(OCH_3)_4$ (206.2)	Calc.	C 52.4	H 8.8	OCH_3 60.2
	Found	» 52.5	» 8.9	» 59.8

The preparation of the 2,5-dimethoxytetrahydrofurans from furan, 2-(acetamido-methyl)-furan, furfuryl methyl ether and methyl 2-furoate has been described previously ^{11, 8, 12, 13}.

Pyrrole. 6.60 g of dimethoxytetrahydrofuran was, during 50 minutes, distilled in a stream of ammonia through a pyrex tube (40 × 1.4 cm) filled with activated aluminum oxide (8–14 mesh, Fisher Scientific Co.). The tube was kept at 250° and connected to a receiver kept at –80°. After the reaction the receiver contained about 10 ml of a liquid, which was heated to 50°, taken up in ether, dried with magnesium sulfate and distilled. Yield 1.78 g of pyrrole = 53 % (yield based upon furan 40 % ^{Cf. 14, 11}); b.p.₇₆₀ = 131–133°; $n_D^{20} = 1.5085$, $n_D^{25} = 1.5068$.

C_4H_5N (67.1)	Calc.	N 20.9
	Found	» 20.9

1-n-Butylpyrrole. 13.2 g of dimethoxytetrahydrofuran (0.10 mole) and 7.30 g of *n*-butylamine (0.10 mole) were dissolved in 20 ml of acetic acid and the solution refluxed for 1 hour. The pyrrole was isolated by addition of 150 ml of water, extraction with 75 ml of ether, washing with water, 2 *M* aqueous potassium hydrogen carbonate and again with water, drying with sodium sulfate and distillation. Yield 3.44 g of 1-*n*-butylpyrrole = 28 % (yield based upon furan = 21 %); colourless liquid with a characteristic odour; b.p.₉ = 52–53°; $n_D^{25} = 1.4700$. Previously found b.p.₁₁ = 53–54° ¹⁵.

$C_8H_{13}N$ (123.2)	Calc.	C 78.0	H 10.6	N 11.4
	Found	» 77.6	» 10.2	» 11.3

1-n-Amylpyrrole. Prepared as 1-*n*-butylpyrrole from 3.30 g of dimethoxytetrahydrofuran (0.025 mole), 2.18 g of *n*-amylamine (0.025 mole) and 5 ml of acetic acid (refluxing time 2 hours). Yield 1.26 g of 1-*n*-amylpyrrole = 37 % (yield based upon furan = 28 %); colourless liquid with a characteristic odour; b.p.₉ = 68–69°; $n_D^{20} = 1.4728$; $n_D^{25} = 1.4701$. Previously found ² b.p.₂₈ = 95–96° and $n_D^{20} = 1.4731$.

$C_9H_{15}N$ (137.2)	Calc.	C 78.8	H 11.0	N 10.2
	Found	» 78.6	» 10.8	» 9.9

1-Phenylpyrrole. 3.30 g of dimethoxytetrahydrofuran (0.025 mole) and 2.33 g of aniline (0.025 mole) were dissolved in 5 ml of acetic acid and the solution refluxed for 1.5 hours and then distilled. Yield 2.68 g of 1-phenylpyrrole = 75 %; b.p.₃₀ = 131–133°; m.p. 57–59° (Hershberg apparatus, corr.). Previously found b.p.₃₈ = 140° ¹⁶ and m.p. 62° ¹⁷.

$C_{10}H_9N$ (143.2)	Calc.	N 9.8
	Found	» 9.9

In another experiment the reactants were heated together without a solvent in a sealed glass tube to 265° for 2 hours. The dark crystalline residue was distilled. Yield 2.80 g of 1-phenylpyrrole = 78 % (yield based upon furan = 59 %); m.p. 55–58°.

1-o-Tolylpyrrole. 6.60 g of dimethoxytetrahydrofuran (0.050 mole) and 5.35 g of *o*-toluidine (0.050 mole) ($n_D^{25} = 1.5697$) were dissolved in 10 ml of acetic acid and the

solution refluxed for 1.5 hours and then distilled. Yield 5.55 g of 1-*o*-tolylpyrrole = 71 % (yield based upon furan = 54 %); b.p.₉ = 97–100°; $n_D^{20} = 1.5711$; $n_D^{25} = 1.5689$. Previously found⁹ b.p.₁₂ = 114° and $n_D^{20} = 1.5749$.

$C_{11}H_{11}N$ (157.2)	Calc.	C 84.0	H 7.1	N 8.9
	Found	» 84.0	» 7.1	» 8.8

1,1'-p-Phenylenedipyrrol. 6.60 g of dimethoxytetrahydrofuran (0.050 mole) and 2.70 g of *p*-phenylenediamine (0.025 mole) were dissolved in 100 ml of acetic acid and the solution refluxed. A precipitate was formed immediately. After 5 minutes another 50 ml of acetic acid was added, 10 minutes later some carbon black was added and again 5 minutes later heating was discontinued and the hot liquid filtered through paper without suction. The filtrate was left standing for 2 hours whereby a crop of crystals separated. The light brown crystals were filtered off, washed with acetic acid and ether and dried. Yield 2.13 g of 1,1'-*p*-phenylenedipyrrol = 41 % (yield based upon furan = 31 %); m.p. 227–230° after sintering at 210°.

$C_{14}H_{12}N_2$ (208.3)	Calc.	C 80.7	H 5.8	N 13.5
	Found	» 80.3	» 5.7	» 13.2

Three crystallizations from acetic acid gave perfectly white crystals, m.p. 229–231°. Sublimation of this product at 0.05 mm did not change the m.p.

Found	C 80.9	H 6.2	N 13.0
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2-Methylpyrrole. 7.30 g of dimethoxytetrahydrofuran was treated with ammonia and worked up as described for the preparation of pyrrole. Yield 2.14 g of a pale yellow liquid, b.p.₁₀ = 43–48°. Redistillation gave 1.51 g of 2-methylpyrrole = 37 % (yield based upon silvan = 25 % *Cf.*⁹); colourless liquid, b.p.₁₀ = 45–47°; $n_D^{20} = 1.5012$; $n_D^{25} = 1.4992$. Previously found b.p.₇₆₀ = 149–150° and $n_D^{20} = 1.5012$ ⁴.

C_5H_7N (81.1)	Calc.	C 74.0	H 8.7	N 17.3
	Found	» 74.0	» 8.7	» 17.3

1-Phenyl-2-methylpyrrole. 3.65 g of dimethoxytetrahydrofuran (0.025 mole) and 2.33 g of aniline (0.025 mole) were dissolved in 5 ml of acetic acid and the solution refluxed for 1.5 hours and then distilled. Yield 3.03 g of 1-phenyl-2-methylpyrrole = 77 % (yield based upon silvan = 51 %); colourless liquid, b.p.₁₁ = 109–111°; $n_D^{20} = 1.5810$; $n_D^{25} = 1.5786$. Previously found b.p.₁₄ = 118–119° and $n_D^{20} = 1.582$ ⁵.

$C_{11}H_{11}N$ (157.2)	Calc.	C 84.0	H 7.1	N 8.9
	Found	» 84.2	» 7.1	» 9.0

1-n-Amyl-2-(acetamidomethyl)-pyrrole. 5.35 g of dimethoxy-2-(acetamidomethyl)-tetrahydrofuran (0.026 mole) and 2.28 g of *n*-amylamine (0.026 mole) were dissolved in 6 ml of acetic acid and the solution refluxed for 30 minutes and then distilled. Yield 4.01 g of 1-*n*-amyl-2-(acetamidomethyl)-pyrrole = 75 % (yield based upon 2-(acetamidomethyl)-furan = 69 % *Cf.*⁸); b.p._{0.1} = 131–134°; m.p. 52–54° (greenish crystals). Redistillation gave 3.44 g of almost colourless crystals with the same m.p. Crystallization of this product from ether gave 2.54 g of white crystals, m.p. 53–55°.

$C_{10}H_{17}N_2(COCH_3)$ (208.3)	Calc.	C 69.2	H 9.7	N 13.5	COCH ₃ 20.7
	Found	» 68.8	» 9.5	» 13.2	» 20.1

Another crystallization from ether gave m.p. 54–56°.

1-Phenyl-2-(methoxymethyl)-pyrrole. 4.40 g of dimethoxytetrahydrofurfuryl methyl ether (0.025 mole) and 2.33 g of aniline (0.025 mole) were mixed and heated to 250° in a sealed glass tube for 3 hours. Distillation gave 1.02 g of crude 1-phenyl-2-(methoxy-

methyl)-pyrrole = 22 % (yield based upon furfuryl methyl ether = 17 % *Cf.12*); colourless liquid, b.p._{0.1} = 71–73°; $n_D^{25} = 1.5668$. Redistillation gave 0.61 g; b.p._{0.1} = 72–73°; $n_D^{25} = 1.5682$. Another distillation did not change the refractive index.

$C_{11}H_{10}N(OCH_3)$ (187.2)	Calc.	C 77.0	H 7.0	N 7.5	OCH_3 16.6
	Found	» 77.3	» 7.1	» 7.6	» 16.6

2-Pyrrolicarboxaldehyde. 4.12 g of dimethoxytetrahydrofurfural dimethyl acetal (0.020 mole) and 1.60 g of ammonium acetate (0.021 mole) were dissolved in 10 ml of acetic acid and the solution refluxed for 15 minutes. The pyrrole was isolated by addition of 20 ml of water, extraction with three 50 ml-portions of ether, drying with sodium sulfate and distillation. Yield 0.61 g of crude 2-pyrrolicarboxaldehyde = 32 % (yield based upon furfural dimethyl acetal = 24 % *Cf.9*); pale-yellow liquid, which crystallizes on cooling; b.p._{0.1} = 55–59°. Crystallization from petroleum ether gave 0.19 g of white crystals, m.p. 43–45°. Previously found 50–51° ¹⁷.

C_5H_5ON (95.1)	Calc.	C 63.1	H 5.3	N 14.7
	Found	» 62.7	» 5.4	» 15.0

A phenylhydrazone was prepared in the usual way. M.p. after two crystallizations from petroleum ether = 139–140°. Previously found 139–140° ¹⁸.

$C_{11}H_{11}N_3$ (185.2)	Calc.	C 71.3	H 6.0	N 22.7
	Found	» 71.7	» 5.9	» 22.4

1-Phenyl-2-pyrrolicarboxaldehyde. 2.06 g of dimethoxytetrahydrofurfural dimethyl acetal (0.010 mole) and 0.93 g of aniline (0.010 mole) were dissolved in 5 ml of acetic acid and the solution refluxed for 30 minutes and then distilled. The resulting pale-yellow liquid (1.14 g) contained 8.4 % of OCH_3 and was apparently a mixture of 1-phenyl-2-pyrrolicarboxaldehyde and the corresponding dimethyl acetal. 0.79 g of the product was refluxed with 3 ml of dioxane and 1 ml of 2 % hydrochloric acid for 3 minutes. 10 ml of water was added and the solution extracted with 10 ml of ether. The ethereal extract was washed quickly with a few ml of 2 *M* aqueous potassium hydrogen carbonate and with water, dried over sodium sulfate and distilled. Yield 0.55 g of 1-phenyl-2-pyrrolicarboxaldehyde = 46 % (yield based upon furfural dimethyl acetal = 35 %); almost colourless liquid, which crystallizes on cooling; b.p._{0.1} = 90–93°; m.p. 27–30°.

$C_{11}H_9ON$ (171.2)	Calc.	C 77.2	H 5.3	N 8.2
	Found	» 76.9	» 5.5	» 7.9

A phenylhydrazone was prepared in the usual way and crystallized twice from ethanol; white crystals, m.p. 130–131°.

$C_{17}H_{15}N_3$ (261.3)	Calc.	C 78.1	H 5.8	N 16.1
	Found	» 78.0	» 5.7	» 16.3

Methyl 2-pyrrolicarboxylate. 4.75 g of methyl dimethoxytetrahydrofuroate (0.025 mole) and 2.00 g of ammonium acetate (0.026 mole) were dissolved in 6 ml of acetic acid and the solution refluxed for 30 minutes. The pyrrole was isolated by addition of 75 ml of water, extraction with 50 ml of ether, washing with water, 2 *M* potassium hydrogen carbonate and again with water, drying with sodium sulfate and distillation. Yield 1.26 g of a colourless liquid, which crystallized on cooling; b.p.₉ = 104–105°. Crystallization from *n*-hexane gave 530 mg of methyl 2-pyrrolicarboxylate = 17 % (yield based upon methyl 2-furoate = 11 % *Cf.13*); m.p. 75–76°. Previously found 73° ¹⁹.

$C_5H_4ON(OCH_3)$ (125.1)	Calc.	C 57.6	H 5.6	N 11.2	OCH_3 24.8
	Found	» 58.0	» 5.4	» 11.2	» 25.0

Methyl 1-phenyl-2-pyrrolicarboxylate. 4.75 g of methyl dimethoxytetrahydrofuroate (0.025 mole) and 2.33 g of aniline (0.025 mole) were dissolved in 5 ml of acetic acid and the solution refluxed for 10 hours. The pyrrole was isolated as in the preceding experiment. Yield 2.87 g of crude methyl 1-phenyl-2-carboxylate = 57 % (yield based upon methyl 2-furoate = 36 %); colourless liquid, which crystallizes; b.p._{0.4} = 105–112°; m.p. 72–78°. Crystallization from methanol gave 1.78 g, m.p. 88–90°.

$C_{11}H_8ON(OCH_3)$ (201.2)	Calc.	C 71.6	H 5.5	N 7.0	OCH_3 15.4
	Found	» 71.9	» 5.8	» 7.1	» 15.6

Another crystallization from methanol gave m.p. 90–91°. Previously found 88°²⁰.

1-Phenyl-3-isopropylpyrrole. 0.90 g of dimethoxy-3-isopropyltetrahydrofuran (0.0052 mole) and 0.48 g of aniline (0.0052 mole) were dissolved in 1.2 ml of acetic acid. The solution was refluxed for 1.5 hours and then distilled. Yield 0.80 g of crude 1-phenyl-3-isopropylpyrrole = 83 % (yield based upon 3-isopropylfuran = 35 %^{Cf.10}); pale-yellow liquid, which crystallizes on cooling; b.p._{0.1} = 89–90°.

$C_{13}H_{15}N$ (185.3)	Calc.	N 7.6
	Found	» 8.0

In order to get the correct analytical values, the compound should be analyzed immediately after distillation. Our purest sample (almost colourless liquid) showed the following data: b.p._{0.1} = 90°; $n_D^{25} = 1.5656$; m.p. 0–2°.

$C_{13}H_{15}N$ (185.3)	Calc.	C 84.3	H 8.2	N 7.6
	Found	» 84.2	» 8.4	» 7.6

Colour reactions. All the above pyrroles gave positive Ehrlich and pine shaving reactions.

SUMMARY

A new method for the transformation of furans into the corresponding pyrroles or N-substituted pyrroles is described.

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