Chemistry of Heterocyclic Compounds, Vol. 40, No. 5, 2004

SYNTHESIS OF N-SUBSTITUTED 5-ALKOXY-3-ARYL-4-METHYL-2,5-DIHYDRO-2-PYRROLONES

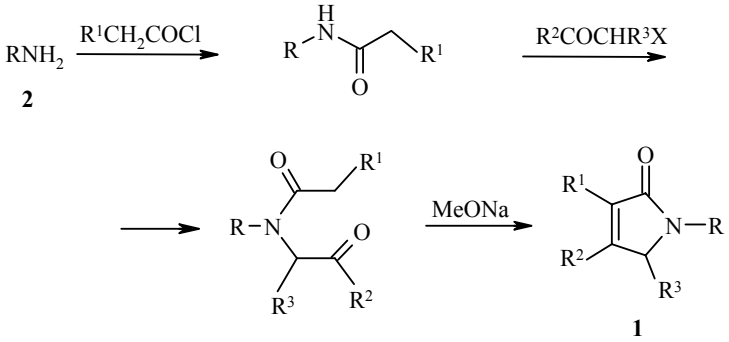
K. V. Nikitin and N. P. Andryukhova

5-Alkoxy-1-aralkyl-3-aryl-4-methyl-2,5-dihydro-2-pyrrolones and the corresponding alkylthio derivatives were synthesized for the first time through the intermediate formation of unsymmetrical maleimides. The possibility of wide variation of the substituents at positions 1, 3, and 5 of the 2-pyrrolones was demonstrated.

Keywords: amido alcohols, herbicides, pyrrolones, ethers.

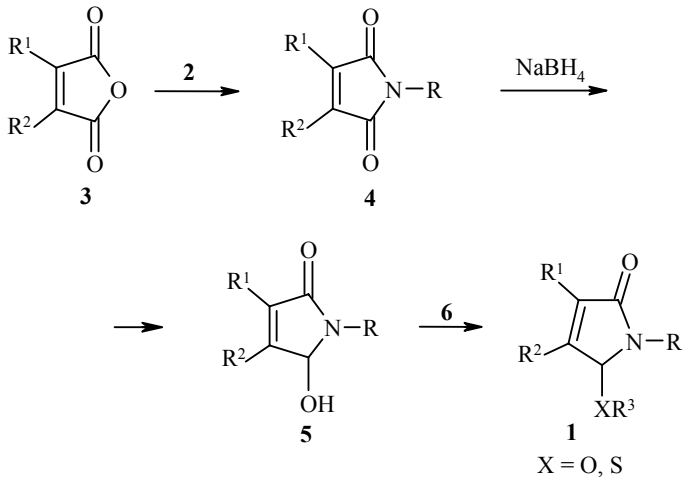
The interest in substituted 2,5-dihydro-2-pyrrolones **1** is due primarily to their application as components of herbicides [1-5]. However, in spite of the fact that many 3,4-homosubstituted pyrrolones **1** ($R^1 = R^2$) have been described [3-5], there is little information on compounds with different substituents at positions 3 and 4 ($R^1 \neq R^2$) and a functional group at position 5 [6].

Two main methods are usually employed for the production of such pyrrolones. The first involves successive acylation of the amine RNH_2 **2** by the action of R^1CH_2COCl followed by alkylation of the obtained amide with the α-halo ketone R^2COCHR^3X and, finally, condensation of the product of the last reaction to the corresponding pyrrolone.



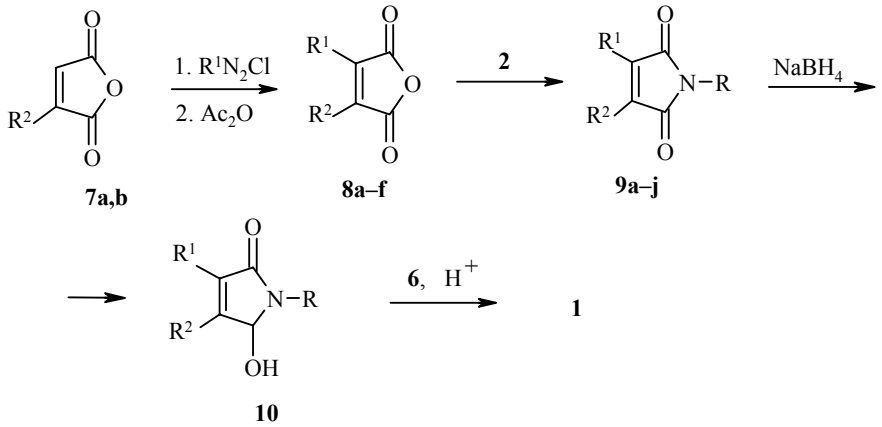
However, the method cannot be used for the synthesis of 5-alkoxy- or 5-alkylthio-substituted pyrrolones. The second method is used for the production of these compounds [3-5], i.e., the symmetrical cyclic anhydride **3** is converted into the symmetrical imide **4** by the action of the amine RNH_2 **2**. The obtained imide **4** is then reduced to the hydroxypyrrolone **5**, and the 5-hydroxy group of the latter is esterified with the corresponding alcohol (X = O) or thiol (X = S) R^3XH **6**.

M. V. Lomonosov Moscow State University, Moscow, Russia; e-mail: newscientist@mtu-net.ru.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 670-678, May, 2004. Original article submitted January 24, 2000; revision submitted April 9, 2001.



The production of pyrrolones **1** through the stage of 3,4-heterosubstituted pyrroles [6] is probably less widely used.

In the present work we describe a new convenient and more general method for the synthesis of 3,4-heterosubstituted pyrrolones **1** that makes it possible to vary widely the substituents at positions 1, 3, and 5 of this heterocycle. The synthesis was conducted by successive arylation of the monosubstituted cyclic anhydride **7a**,**b**, imidation of the obtained unsymmetrical anhydride **8** with the primary amine **2**, reduction of the obtained imide **9** to the N-substituted 3-aryl-5-hydroxy-4-methyl-2,5-dihydro-2-pyrrolone **10**, and finally substitution of the hydroxyl in the latter by the OR^3 or SR^3 group by the action of alcohol or thiol **6** on the hydroxypyrrolone **5** with the formation of the final pyrrolone **1**.



7 a R^2 = H, **b** R^2 = Me

The unsymmetrical anhydrides **8a-f** were obtained in the Meerwein reaction [7] by the reaction of arenediazonium chloride with monosubstituted anhydrides **7a**,**b** in acetone with copper salts as catalysts (Table 1). The intermediately formed 3-aryl-4-chloro-4-methylsuccinic anhydrides were not isolated but were subjected directly to elimination of HCl in boiling acetic anhydride. The obtained unsymmetrical maleic anhydrides **8a-f** were purified by vacuum distillation. It should be noted that alternative methods for the synthesis of the anhydrides **8** have been described in the literature. One of them is based on pyrolysis of the relatively inaccessible 1-ethoxyalkenyl esters of α-keto acids [8]. In our case methods based on the condensation of arylacetonitriles R^1CH_2CN and α-keto acids [9] or phenylacetic acids with α-keto acids [10] did not give the desired results.

TABLE 1. The Characteristics of the Unsubstituted Maleic Anhydrides **8a-f**

Compound*	R^1	Empirical formula	Found, % / Calculated, %		bp, °C (0.01 mm Hg)	mp, °C	IR spectrum ν, cm^{-1} (CO)	^{1}H NMR spectrum, δ, ppm	Yield, %
			C	H					
8a	Ph	$C_{11}H_8O_3$	—	—	130-135	92 (94 [8])	1750	2.3 (3H, s); 7.6 (5H, m)	32
8b	2-FC_6H_4	$C_{10}H_5FO_3$	62.30 / 62.51	2.77 / 2.62	120	68	1758	7.18-7.38 (3H, m); 7.50-7.65 (1H, m); 8.34 (1H, s)	41
8c	2-FC_6H_4	$C_{11}H_7FO_3$	64.42 / 64.08	3.13 / 3.42	127	45	1755	2.18 (3H, s); 7.2-7.6 (4H, m)	65
8d	3-FC_6H_4	$C_{11}H_7FO_3$	63.88 / 64.08	3.44 / 3.42	125	44	1750	2.33 (3H, s); 7.1-7.6 (4H, m)	58
8e	3-Cl-4-FC_6H_3	$C_{11}H_6ClFO_3$	55.09 / 54.91	2.70 / 2.51	145-150	—	1758	2.33 (3H, s); 7.0-7.8 (3H, m)	31
8f	4-Cl-2F-C_6H_3	$C_{11}H_6ClFO_3$	55.34 / 54.91	2.66 / 2.51	148-155	—	1760	2.27 (3H, s); 7.0-7.7 (3H, m)	38

* **8 a,c-f** R^2 = Me, **b** R^2 = H.

TABLE 2. The Characteristics of the Unsubstituted Maleimides **9a-j**, Obtained from the Anhydrides **8a-f** and Amines **2**

Compound*	R^1	R	Empirical formula	Found, % / Calculated, %			mp, °C	^{1}H NMR spectrum, δ, ppm (*J*, Hz)	Yield, % (method)*[2]
				C	H	N			
9a	H	$PhCH_2$	$C_{12}H_{11}NO_2$	—	—	—	*[3]	2.03 (3H, s); 4.6 (2H, s); 6.28 (1H, s); 7.3 (5H, m)	90 (A)
9b	Ph	$PhCH_2$	$C_{18}H_{15}NO_2$	77.68 / 77.96	5.60 / 5.45	4.97 / 5.05	70	2.03 (3H, s); 4.73 (2H, s); 7.1-7.5 (10H, m)	82 (A)
9c	2-FC_6H_4	$PhCH_2$	$C_{18}H_{14}FNO_2$	73.31 / 73.21	4.89 / 4.78	4.66 / 4.74	74	2.06 (3H, s); 4.73 (2H, s); 7.1-7.50 (9H, m)	86 (A)
9d	2-FC_6H_4	3-$ClC_6H_4CMe_2$	$C_{20}H_{17}ClFNO_2$	67.28 / 67.14	5.00 / 4.79	3.97 / 3.91		1.96 (6H, s); 2.02 (3H, s); 7.05-7.5 (8H, m)	45 (B), 78 (B)
9e	2-FC_6H_4	3,5-$Cl_2C_6H_3CMe_2$	$C_{20}H_{16}Cl_2FNO_2$	60.93 / 61.24	4.50 / 4.11	3.55 / 3.57	106	1.94 (6H, s); 2.03 (3H, s); 7.2 (5H, m); 7.6 (2H, m)	55 (B)
9f	3-FC_6H_4	3,5-$Cl_2C_6H_3CMe_2$	$C_{20}H_{16}Cl_2FNO_2$	60.99 / 61.24	4.24 / 4.11	3.43 / 3.57	108	1.95 (6H, s); 2.02 (3H, s); 7.2-7.6 (7H, m)	50 (B)
9g	4-Cl-2FC_6H_3	3,5-$Cl_2C_6H_3CMe_2$	$C_{20}H_{15}Cl_3FNO_2$	56.12 / 56.30	3.44 / 3.54	3.23 / 3.28		1.93 (6H, s); 2.02 (3H, s); 7.2-7.5 (6H, m)	48 (B)
9h	Ph	3,5-$Cl_2C_6H_3CMe_2$	$C_{20}H_{17}Cl_2FNO_2$	64.00 / 64.18	4.90 / 4.58	4.02 / 3.74		1.93 (6H, s); 2.15 (3H, s); 7.22 (3H, s); 7.4-7.6 (5H, m)	84 (B)
9i	H	2-F-4-Cl-5-HOC_6H_2	$C_{11}H_7ClFNO_3$	51.60 / 51.66	2.69 / 2.76	5.26 / 5.48	171	2.18 (3H, s); 5.72 (1H, s); 6.53 (1H, s); 6.90 (1H, d, *J* = 6.5); 7.23 (1H, d, *J* = 9.1)	75 (A)
9j	Ph	2-F-4-Cl-5-HOC_6H_2	$C_{17}H_{11}Cl_3FNO_3$	61.61 / 61.55	3.51 / 3.34	4.27 / 4.22	166	2.30 (3H, s); 5.7 (1H, br. s); 6.99 (1H, d, *J* = 6.5); 7.33 (1H, d, *J* = 7.9); 7.5-7.7 (5H, m)	50 (A)

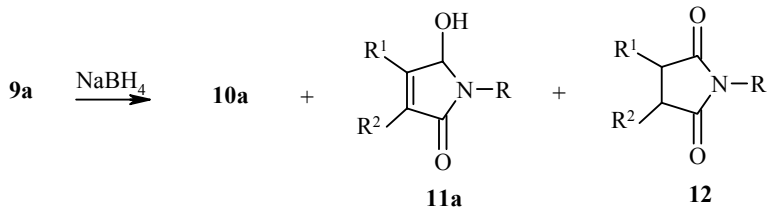
* **9a-j** R^2 = Me.

*[2] A is the method described in [1]; B is 2 mol of acetic acid in dioxane; C is 1 mol of acetic acid and 1 mol of triethylamine in benzene.

*[3] bp 130°C (1 mm Hg); the boiling point was not given in [11].

The transition from the unsymmetrical anhydrides **8a-f** to the maleimides **9** is usually realized with good yields [3-5, 11] by refluxing them with amines **2** in acetic acid. Direct alkylation of the maleimides **9** (R = H) with alcohols in the presence of triphenylphosphine also gives good results. It is surprising that the authors of [11] used alkylation of the silver salt of citraconimide for the synthesis of the N-benzylimide of citraconic acid **9a** with a yield of 24%, whereas we obtained the imide **9a** by the usual method (with a yield of 88%). The imidation of arylmethylmaleic anhydrides **8a-c** with benzylamine also does not give rise to any complications (Table 2), but the corresponding acetanilide is formed as side product if substituted anilines are used in the reaction. In the reaction of the anhydride **8c** with α,α-dimethyl-3-chlorobenzylamine in acetic acid (method A [11]) the corresponding imide is hardly formed at all, and the reaction takes place with a satisfactory yield only if 2 eq. of acetic acid in dioxane is used (method B). With the use of 1 mol of triethylamine and 1 mol of acetic acid to 1 mol of the anhydride in benzene (method C) the yield of the imide becomes high. The restricted formation of the imides from amines in which the NH_2 group is attached to a tertiary carbon atom can probably be explained by steric hindrances to nucleophilic attack by such an amine on the carbonyl groups of the anhydride.

The reduction of the imides **9a-j** to the corresponding hydroxypyrrolones was realized with sodium borohydride in methanol [3-5], since it is known that the same reaction in THF [11] leads to the formation of side products. Reduction of the imides **9** under our conditions leads to the formation of a mixture of two regioisomeric cyclic N-substituted amido alcohols: 3-Aryl-4-methyl-1,5-dihydro-2H-pyrrol-2-one **10** and 4-aryl-3-methyl-1,5-dihydro-2H-pyrrol-2-one **11**. During reduction of the imide **9a** the succinimide **12** is formed in addition.



The structure of the individual isomeric pyrrolones **10a** and **11a** was established by 2D ^{1}H NMR and ^{1}H NOE. The acyclic aldehyde form was not found in the reaction mixture.

TABLE 3. The Reduction of the Imides **9a-j** by Sodium Borohydride in Methanol

Imide	$NaBH_4$, mol	**10** : **11**	Yield, %	
			10a–j	**11a–j**
9a	0.5	8:1	76	10*
9b	1	1:1	43	53
9c	0.5	2:1	61	34
9d	1	3.5:1	62	18
9e	1	3.5:1	58	16
9f	1	4:1	66	17
9g	1	3.5:1	53	15
9h	1	3.5:1	76	23
9i	1	5:1	70	14
9j	1.5	2:1	55	25

* In addition, 12% of N-benzylmethylsuccinimide is formed.

TABLE 4. Characteristics of the Synthesized Substituted 4-Methyl-1,5-dihydro-2H-pyrrol-2-ones **1a-l***

Compound*[2]	R	R^3	Empirical formula	Found, % / Calculated, %			^{1}H NMR spectrum, δ, ppm (*J*, Hz)	Yield, %
				C	H	N		
1a	$PhCH_2$	Me	$C_{13}H_{15}NO_2$	71.55 / 71.87	7.07 / 6.96	6.33 / 6.45	1.95 (3H, s); 2.98 (3H,s); 4.04 (1H, d, *J* = 14.8); 4.95 (1H, d, *J* = 14.8); 5.02 (1H, s); 5.95 (1H, s); 7.29 (5H, s)	92
1b	$PhCH_2$	CH_2CH_2Cl	$C_{14}H_{16}ClNO_2$	63.40 / 63.28	6.22 / 6.07	5.20 / 5.27	1.92 (3H, s); 3.2–3.5 (4H, m); 4.12 (1H, d, *J* = 15); 4.8 (1H, d, *J* = 15); 5.06 (1H, s); 5.89 (1H, s); 7.25 (5H, s)	97
1c	$PhCH_2$	Me	$C_{19}H_{19}NO_2$	77.59 / 77.79	6.68 / 6.53	4.85 / 4.77	2.07 (3H, s); 3.03 (3H, s); 4.13 (1H, d, *J* = 14.8); 5.05 (1H, d, *J* = 14.8); 5.11 (1H, s); 7.2–7.6 (10H, m)	90
1d	3,5-$Cl_2C_6H_3CMe_2$	Me	$C_{21}H_{21}Cl_2NO_2$	64.77 / 64.62	5.30 / 5.42	3.60 / 3.59	1.74 (3H, s); 1.84 (3H, s); 2.14 (3H, s); 3.17 (3H, s); 5.6 (1H, s); 7.2-7.6 (8H, m)	92
1e	3,5-$Cl_2C_6H_3CMe_2$	Et	$C_{22}H_{23}Cl_2NO_2$	65.60 / 65.35	5.49 / 5.73	3.64 / 3.46	1.26 (3H, m); 1.7 (3H, s); 1.85 (3H, s); 2.15 (3H, s); 3.2-3.5 (2H, m); 5.6 (1H, s); 7.2-7.6 (8H, m)	90
1f	3,5-$Cl_2C_6H_3CMe_2$	*i*-Pr	$C_{23}H_{25}Cl_2NO_2$	65.91 / 66.03	6.17 / 6.02	3.29 / 3.35	1.18 (3H, d, *J* = 6.1); 1.27 (3H, d, *J* = 6.1); 1.75 (3H, s); 1.87 (3H, s); 2.19 (3H, s); 3.97 (1H, m); 5.6 (1H, s); 7.15-7.6 (8H, m)	87
1g	$PhCH_2$	CH_2CH_2Cl	$C_{20}H_{20}ClNO_2$	70.03 / 70.27	6.11 / 5.90	3.88 / 4.10	2.11 (3H, s); 3.3-3.6 (4H, m); 4.30 (1H, d, *J* = 14.5); 4.98 (1H, d, *J* = 14.5); 5.22 (1H, s); 7.2-7.6 (10H, m)	95
1h	3,5-$Cl_2C_6H_3CMe_2$	Et	$C_{22}H_{23}Cl_2NOS$	63.00 / 62.85	5.45 / 5.51	3.25 / 3.33	1.16 (3H, t, *J* = 7.5); 1.87 (3H, s); 1.94 (3H, s); 2.14 (2H, q, *J* = 7.5); 2.23 (3H, s); 5.18 (1H, s); 7.2-7.5 (8H, m)	95
1i	3,5-$Cl_2C_6H_3CMe_2$	C_6H_{11}-*cyclo*	$C_{26}H_{29}Cl_2NOS$	66.08 / 65.81	6.06 / 6.16	3.00 / 2.95	1.1-1.5 (6H, m); 1.5-1.8 (4H, m); 1.87 (3H, s); 1.95 (3H, s); 2.24 (3H, s); 2.25 (1H, m); 5.20 (1H, s); 7.2-7.4 (8H, m)	96
1j	3,5-$Cl_2C_6H_3CMe_2$	CH_2COOEt	$C_{24}H_{25}Cl_2NO_4$	62.28 / 62.34	5.62 / 5.45	2.80 / 3.03	1.30 (3H, t, *J* = 7); 1.80 (3H, s); 1.87 (3H, s); 2.17 (3H, s); 3.76 (1H, d, *J* = 14); 4.02 (1H, d, *J* = 14); 5.79 (1H, s); 7.2-7.5 (8H, m)	70
1k	2F-4Cl-5HOC_6H_2	CH_2CH_2Br	$C_{13}H_{12}BrClFNO_3$	42.44 / 42.83	3.10 / 3.32	3.91 / 3.84	2.15 (3H, s); 3.3-3.7 (4H, m); 5.85 (1H, s); 6.1 (1H, s); 7.0-7.2 (2H, m); 7.4 (1H, s)	91
1l	$PhCH_2$	Me	$C_{19}H_{18}FNO_2$	72.92 / 73.29	5.63 / 5.83	4.26 / 4.50	1.94 (3H, s); 3.06 (3H, s); 4.16 (1H, d, *J* = 14.6); 5.04 (1H, d, *J* = 14.6); 5.16 (1H, s); 7.05-7.50 (9H, m)	90

* Compounds **1a-l** are thick oils.

*[2] **1a,b,k** R^1 = H, **c-j** R^1 = Ph, **l** R^1 = 2-FC_6H_4; **a-l** R^2 = Me.

In order to avoid inaccuracies in the separation of the isomeric pyrrolones **10** and **11** the ratio of the reduction products was determined by ^{1}H NMR spectroscopy from the ratio of the signals for the protons at position 5 of the pyrrolone ring. For compounds **10** the position of this signal is 0.5-0.6 ppm downfield from the signal for compounds **11**. The ratio of the hydroxypyrrolones **10** and **11**, determined by NMR, agrees well with the yields of the individual 5-alkoxypyrrolones **1** isolated from mixtures of the isomers **10** and **11** (Table 3).

During investigation of this reaction we established that the pyrrolones **10** are mostly formed, but the selectivity of reduction is low, and sometimes the pyrrolone **11** (reduction of the imide **9b**) predominates in the mixture. The reduction of the citraconimides **9a** and **9i** is most selective. These imides, which do not have substituents at position 3, probably have the most symmetric distribution of electron density of the π-system, characterized by a relatively low electron density at position 5, to which attack by the reducing agent is mostly directed. Conversely, reduction of N-benzyl-3-methyl-4-phenylmaleimide **9b**, where the phenyl substituent has a +M effect, gives mostly the pyrrolone **11b**. Nevertheless, all the imides with tertiary benzyl or aromatic substituents at the nitrogen atom **9d-j** are reduced fairly selectively with the formation of the isomeric pyrrolones **10d-j** and **11d-j** in ratios (3:1)-(5:1).

The target products – the pyrrolones **1** (Table 4) – are easily formed during treatment of the respective compounds **10** with an excess of the primary or secondary alcohol with protic acids (HCl, TsOH) as catalysts. Tertiary alcohols do not enter into the reaction, as we demonstrated for the case of *tert*-butyl alcohol. The transformation of the pyrrolones **11** into the alkylated derivatives **1** takes place readily under the same conditions. It is possible, therefore, not to separate the highly polar compounds **10** and **11** but to separate their isomeric alkoxylation products **1**. An interesting feature of the NMR spectra of compounds **1a-c**,**g**,**l** should be mentioned (Table 4). The signals of the diastereotopic protons of the methylene group of the benzyl radical in these compounds are separated from each other by 0.8-1.0 ppm with spin–spin coupling constant 14-15 Hz in spite of the fact that the asymmetric carbon atom is three bonds away from these protons. A possible explanation of the such a strong effect of the asymmetry on the chemical shift may be that the nitrogen atom in these systems has a nonplanar configuration and itself becomes asymmetric.

The formation of the alkylthiopyrrolones **1** in the reaction of hydroxypyrrolones **10** with thiols is similar to the reaction of the latter with alcohols but takes place noticeably more readily. A small excess of the thiol is sufficient to complete the reaction.

The ease of substitution of the hydroxyl at position 5 in the investigated 1,5-dihydro-2H-pyrrol-2-ones is probably due to the formation an intermediate carbenium-immonium cation during the action of the acids on them. Nevertheless, in a number of cases alkylation of the free hydroxyl of the 5-hydroxy-1,5-dihydro-2H-pyrrol-2-one with the respective halide ($ClCH_2COOEt$) proved more successful for the introduction of a substituent at position 5 (for example OCH_2COOEt).

Thus, it is possible by the proposed method to produce a wide range of compounds **1** by varying the substituents at positions 1, 3, and 5.

EXPERIMENTAL

The ^{1}H NMR spectra were measured on a Varian GEMINI-200 instrument (200 MHz) in deuterochloroform with TMS as internal standard. The mass spectra were obtained on a GCMS-OP 1000 instrument. The IR-FT spectra were recorded on a Mattson Genesis II spectrophotometer. Chromatographic separation of the mixtures was performed on Merck silica gel 40/63 μ. The eluant was hexane–ethyl acetate. The melting points were determined on Thomas-Hoover capillary equipment and were not corrected. The commercial reagents and solvents were used without further purification.

The characteristics of the synthesized compounds are given in Tables 1-4.

Unsymmetrical Maleic Anhydrides (8a-f) (General Procedure). To conc. hydrochloric acid (8 ml, 0.1 mol) we added water (15 ml) and substituted aniline (50 mmol). The mixture was cooled to 3°C, and a saturated aqueous solution of sodium nitrite (3.45 g, 50 mmol) was added drop by drop. Then a solution of copper chloride (1.34 g, 10 mmol) and the anhydride **7** (5.6 g, 50 mmol) in a mixture of water (2 ml) and acetone (20 ml) was added. The reaction mixture was stirred at 5°C for 2 h and then at room temperature for 20 h. The bottom layer was rejected, and the top layer was evaporated under vacuum, and 30 ml of acetic anhydride was added to the residue. The mixture was refluxed for 12 h and submitted to fractional distillation under vacuum, and the last fraction was collected.

Unsymmetrical Maleimides (9a-j). A. To a solution of the anhydride **8** (1 mmol) in acetic acid (1 ml) we added the amine **2** (1 mmol). The mixture was refluxed for 12 h, and the reaction product was isolated by vacuum distillation or chromatography.

B. To a solution of the anhydride **8** (1 mmol) in dioxane (2 ml) we added acetic acid (2 mmol) and then the amine **2** (1 mmol). The mixture was refluxed for 12 h, and the reaction product was isolated by vacuum distillation or chromatography.

C. To a solution of the anhydride **8** (1 mmol) in benzene (2 ml) we added acetic acid (1 mmol), triethylamine (1 mmol), and then the amine **2** (1 mmol). The mixture was refluxed for 12-24 h, and the reaction product was isolated by vacuum distillation or chromatography.

3,4-Disubstituted 5-Hydroxy-1,5-dihydro-2H-pyrrol-2-ones (10a-j, 11a-j) (General Procedure). In methanol (80 ml) in an atmosphere of nitrogen at 40°C we dissolved the hydroxypyrrolone **9** (10 mmol). With stirring we then added slowly sodium borohydride (0.38 g, 10 mmol). The reaction mixture was evaporated under vacuum, and water (10 ml) was added. The product was extracted with ethyl acetate (for compounds **9i**,**j** the pH of the aqueous phase was previously brought to 6-7), washed with ammonium chloride solution, dried, and evaporated. The mixture of isomers **10** and **11** was used without further purification. They can be isolated in the individual form by chromatography on silica gel.

3,4-Disubstituted 5-Alkoxy-1,5-dihydro-2H-pyrrol-2-ones and 3,4-Disubstituted 5-Alkylthio-1,5-dihydro-2H-pyrrol-2-ones (1a-l). General Procedure for the Volatile Alcohols. To compound **10** (1 mmol) (containing the isomer **11** as impurity) we added the respective alcohol (5 ml) and *p*-toluenesulfonic acid (0.019 g, 0.1 mmol). The mixture was refluxed for 1 h, and triethylamine (0.1 ml, 0.72 mmol) was added. The mixture was evaporated under vacuum, and ethyl acetate (10 ml) was added. The mixture was washed with water, dried, and evaporated, and the reaction product (**1**) was purified by chromatography.

General Procedure for the Nonvolatile Alcohols and Thiols. To compound **10** (1 mmol) we added benzene (5 ml), the respective alcohol (2 mmol) (1.1 mmol of the thiol), and *p*-toluenesulfonic acid (0.019 g, 0.1 mmol). The mixture was refluxed for 4 h, and triethylamine (0.1 ml, 0.72 mmol) and ethyl acetate (10 ml) were added. The product was washed with water, dried, evaporated, and purified by chromatography.

REFERENCES

1. K. Moriyasu, H. Akieda, H. Aoki, M. Suzuki, S. Matsuto, Y. Iwasaki, S. Koda, and K. Tomiya, US Patent 5409886; *Chem. Abstr.*, **124**, P8680 (1995).
2. N. Ohba, A. Ikeda, K. Matsunari, Y. Yamada, M. Hirata, Y. Nakamura, A. Takeuchi, and H. Karino, US Patent 5006157; *Chem. Abstr.*, **114**, 247145 (1991).
3. B. Boehner and M. Baumann, Swiss. Pat. 633678; *Chem. Abstr.*, **98**, 121386 (1983).
4. B. Boehner and M. Baumann, German Patent 2735841; *Chem. Abstr.*, **88**, 152415 (1978).
5. T. Kume, T. Goto, M. Honmachida, A. K. Amochi, A. Yanagi, S. Yagi, and S. Miyachi, European Patent 0286816 (1988); *Chem. Abstr.*, **110**, 135246 (1989).
6. H. Kinoshita, Y. Hayashi, Y. Murata, and K. Inomata, *Chem. Lett.,* 1437 (1993).
7. C. S. Rondestvedt and O. Vogl, *J. Am. Chem. Soc.*, **77**, 2313 (1955).

8. M. S. Newman and W. M. Stallick, *J. Org. Chem.*, **38**, 3386 (1973).
9. W. D. Dean and D. M. Blum, *J. Org. Chem.*, **58**, 7916 (1993).
10. E. K. Fields, S. J. Behrend, S. Meyerson, M. L. Winzenburg, B. R. Ortega, and H. K. Hall, *J. Org. Chem.*, **55**, 5165 (1990).
11. G. B. Gill, G. D. James, K. V. Gates, and G. Pattenden, *J. Chem. Soc. Perkin Trans. 1*, 2567 (1993).
12. F. Farina, M. V. Martin, and M. C. Paredes, *Heterocycles*, **22**, 1733 (1984).