Tandem transformations of tetrahydropyrrolo[3,2-*c*]pyridines under the action of dimethyl acetylenedicarboxylate. A novel route to pyrrolo[2,3-*d*]azocines

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Reactions of substituted tetrahydropyrrolo[3,2-*c*]pyridines with dimethyl acetylenedicarboxylate in protic and aprotic solvents were studied. A novel single-step method for the synthesis of pyrrolo[2,3-*d*]azocine derivatives was developed.

Key words: tetrahydropyrrolo[3,2-*c*]pyridines, tandem opening, pyrrolo[2,3-*d*]azocines.

Opening of the piperidine ring occurs in three known reactions that require heating: the Hofmann reaction[1] and the Braun reactions[2] (opening of *N*-benzoylpiperidines under the action of phosphorus pentahalides and *N*-alkylpiperidines under the action of cyanogen bromide). These reactions are of no preparative value because the resulting compounds can be obtained more easily and in higher yields from more accessible starting reagents. The Hofmann reaction is often used to determine the location of substituents in the piperidine fragment of various alkaloids.[3] Dimethyl acetylenedicarboxylate is widely employed in the chemistry of nitrogen-containing heterocyclic compounds for annelation of five-, six-, and seven-membered fragments.[4] In reactions of 1-alkyl- or 1-arylalkyl-1,4,5,6-tetrahydropyridines with dimethyl acetylenedicarboxylate and ethyl propiolate in boiling benzene, the six-membered ring extends to a tetrahydroazocine one.[5] Recently, we have described first examples of opening of the tetrahydropyridine fragment in tetrahydropyrrolo[3,2-*c*]pyridines (THPP) under the action of acetic anhydride[6] at 70 °C and dimethyl acetylenedicarboxylate[7—9] at 20 °C. In the latter case, substituted 2- or 3-vinylpyrroles and tetrahydropyrrolo[2,3-*d*]azocines[7,8] were obtained in aprotic solvents and 3-alkoxy(hydroxy)alkylpyrroles,[9] in alcohols and aqueous THF (Scheme 1).

In the present paper, we discuss tandem reactions of THPP with dimethyl acetylenedicarboxylate (DMAD) in various solvents. We examined tetrahydropyrrolo[3,2-*c*]pyridines **1**—**15** with different substituents at the N and C atoms of the tetrahydropyridine fragment and at the N and α-C atoms of the pyrrole fragment. Their synthesis has been described earlier.[10,11] Benzene, anhydrous THF, acetonitrile, DMSO, acetone, and carbon disulfide were used as aprotic solvents and methanol, ethanol, aqueous THF, and aqueous dioxane were used as protic solvents. The results obtained are presented in Scheme 1 and Table 1.

In aprotic solvents, the reactions of compounds **1**—**6** with DMAD were completed in 4—9 h and those of compounds **13**—**15**, in 10—24 h. In protic solvents, the reac-

Table 1. Character and yields of products in the reactions of tetrahydropyrrolopyridines **1**—**7**, **13**, and **14** with DMAD in various solvents

Starting reagent	Solvent	Yields of the products (%)	
		VP*	PA**
1	Benzene	76 (**16**)	—
	THF (anhydrous)	30 (**16**)	—
2	Benzene	90 (**17**)	—
	THF (anhydrous)	35 (**17**)	14 (**24**)
	Acetonitrile	40 (**17**)	35 (**24**)
	DMSO	35 (**17**)	14 (**24**)
3	Benzene	56 (**18**)	28 (**25**)
	THF (anhydrous)	32 (**18**)	20 (**25**)
	Acetonitrile	45 (**18**)	28 (**25**)
	DMSO	29 (**18**)	17 (**25**)
	Acetone	49 (**18**)	22 (**25**)
4	THF (anhydrous)	41 (**19**)	10 (**26**)
	Acetonitrile	43 (**19**)	20 (**26**)
5	THF (anhydrous)	32 (**20**)	—
	Acetonitrile	81 (**20**)	—
6	THF (anhydrous)	53 (**21**)	—
7	THF (anhydrous)	44 (**22**)	—
13	THF (anhydrous)	62 (**23**)	—
14	Benzene	—	15 (**28**)
	Acetonitrile	—	42 (**28**)
	CS_2	—	40 (**28**)

* 3-Vinylpyrrole.
** Pyrroloazocine.

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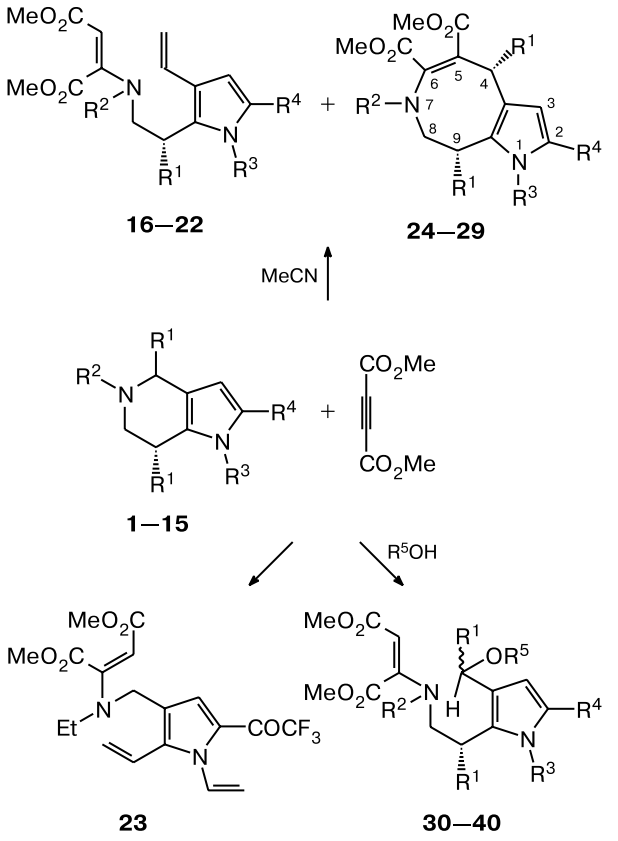
Scheme 1



Compound	Product	R^1	R^2	R^3	R^4
1	**16**	Me	Me	H	H
2	**17**, **24**, **30**	Me	Me	H	CHO
3	**18**, **25**, **31**	Me	Me	H	CF_3CO
4	**19**, **26**	Me	Me	H	$CH{=}C(CN)_2$
5	**20**, **27**, **32**	Me	Me	H	MeCO
6	**21**	Me	Me	H	$CH{=}C(CN)CO_2Et$
7	**22**	Me	Me	$CH{=}CH_2$	H
8	**34**	Me	Me	$CH{=}CH_2$	CH_2OH
9	**35**	Me	Me	$CH{=}CH_2$	$CH{=}C(CN)_2$
10	**36**	Me	Me	$CH{=}CH_2$	CHO
11	**33***	Me	Me	H	CH_2NMe_2 (**11**), CH_2OMe (**33**)
12	**	Me	Me	$CH{=}CH_2$	H_2CN⟨O⟩
13	**23**, **37**, **40**	H	Et	$CH{=}CH_2$	CF_3CO
14	**28**, **38**	H	Bn	H	CF_3CO
15	**29**, **39**	H	Bn	$CH{=}CH_2$	CF_3CO

* The reaction in MeOH yielded compound **33**; in aprotic solvents, dimethyl 2-dimethylaminobut-2-enedioate was obtained.

** In aprotic solvents, dimethyl 2-morpholinobut-2-enedioate was obtained.

R^5 = Et (**30**, **31**), Me (**32—35**, **38—40**), H (**36**, **37**)

tion times were 2—4 and 4—8 h, respectively. In benzene, the major products from compounds **1** and **2** were the corresponding 3-vinylpyrroles **16** and **17**. The presence of a strong electron-withdrawing trifluoroacetyl group in position 2 causes a competitive reaction leading to pyrrolo[2,3-*d*]azocine **25** (see Table 1). The reaction with compound **14** containing no substituents at the C atoms in the tetrahydropyridine ring gave under these conditions only azocine **28** in low yield.

In other polar solvents (THF, acetonitrile, DMSO, and acetone), compounds **2**—**4** with electron-withdrawing substituents in position 2 yielded mixtures of the corresponding vinylpyrroles **17**—**19** and pyrroloazocines **24**—**26** in different ratios (see Table 1).

The tandem transformation in the reactions of compounds **5** and **6** with DMAD in THF (also in acetonitrile for compound **5**) gave rise only to 3-vinylpyrroles **20** and **21**.

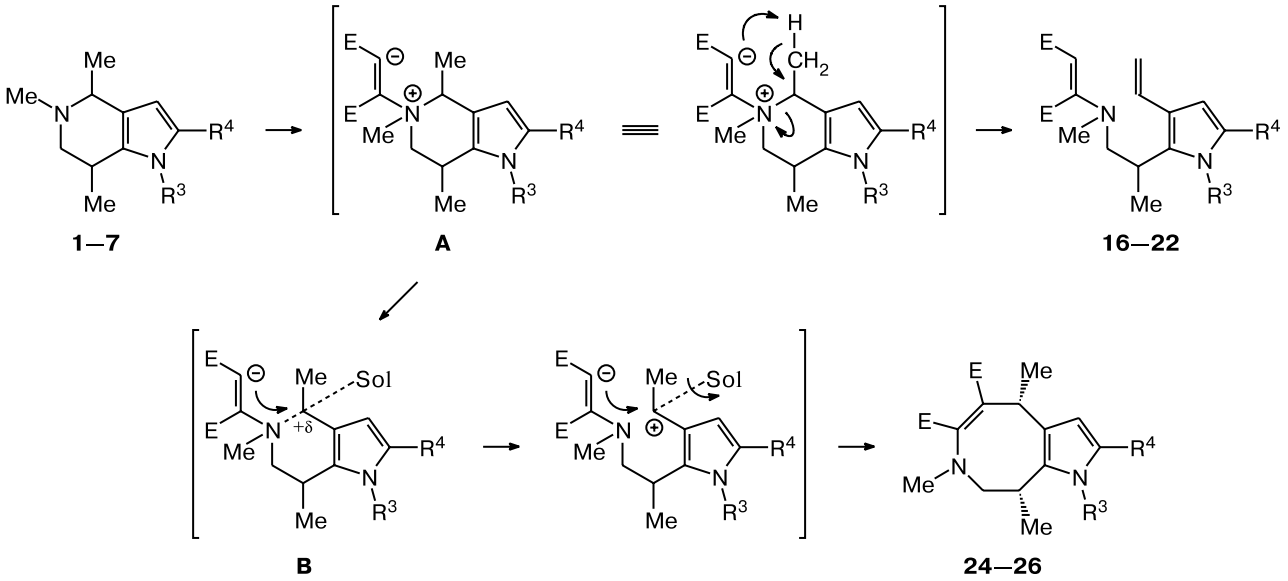
In the reactions of compounds **11** and **12** with DMAD in aprotic solvents, the dimethylamine and morpholine fragments were eliminated to give dimethyl 2-dimethylamino- and 2-morpholinobut-2-enedioates in 79 and 82% yields, respectively. We failed to determine the geometries of the esters obtained and follow the transformation pathways of the pyrrolopyridine fragment.

The reaction of 5-benzyl-2-trifluoroacetyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridine (**14**) containing the C-unsubstituted tetrahydropyridine ring with DMAD in benzene, acetonitrile, and carbon disulfide gave pyrroloazocine **28** in 15—42% yield. 3-Vinyl- and 1,3-divinylpyrroles **22** and **23** were obtained from *N*-vinylpyrroles **7** and **13** in THF in sufficiently high yields.

The aforementioned effect of the structure of THPP on the ease and pathway of their reactions with DMAD in aprotic solvents is consistent with the suggested Scheme 2 including an attack of the N atom of the tetrahydropyridine fragment on the triple bond of DMAD. The transformation of an intermediate ammonium zwitterion of the type **A** is determined by the polarity and nucleophilicity of the solvent used.

In benzene, the anionic center of zwitterion **A** loses the proton of the methyl group in position 4 to form 3-vinylpyrroles **16**—**22** *via* the Hofmann opening of the tetrahydropyridine fragment in compounds **1**—**7**. The aprotic solvents THF, DMSO, acetonitrile, acetone, and carbon disulfide having the atoms with lone electron pairs favor cleavage of the C(4)—N by their nucleophilic assistance. In such solvents, zwitterion **A** can transform into an intermediate of the type **B**, through which THPP can undergo competitive transformations. This is followed by a reaction between ions or nucleophilic displacement of the solvent by an anion to give pyrroloazocines **24**—**26** in 10 to 35% yields. This process is accompanied by an inversion of configuration at the C(4) atom. According to

Scheme 2



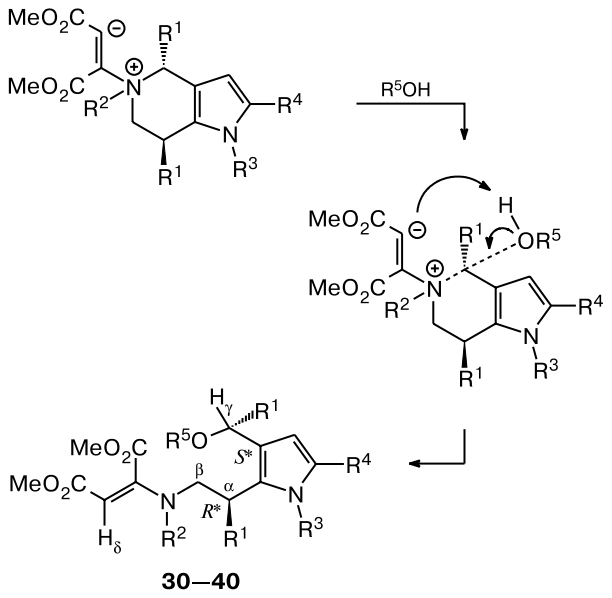
E = CO_2Me

X-ray diffraction data,[8] the methyl groups at C(4) and C(9) in pyrroloazocines **24**—**26** are *cis*-arranged. In the case of THPP **2**—**4**, the total yields of 3-vinylpyrroles and pyrroloazocines ranged from 46 to 75%. The presence of trifluoroacetyl group makes it possible to transform compounds **3** and **14** into the corresponding azocines **25** and **28** in benzene. Because the positive charge upon the cleavage of the C(4)—N bond in the transition state **B** is delocalized at the C(4) atom, the electron-donating substituents facilitate the process. That is why 4-methyl-THPP **2**—**4** transform into pyrroloazocines more easily than does unsubstituted compound **14**. It should be noted that the reactions of *N*-vinyltetrahydropyrrolopyridines **7**—**10**, **13**, and **15** with DMAD in polar aprotic solvents did not yield the corresponding 1-vinylpyrroloazocines. Apparently, this is due to the electron-withdrawing effect of the vinyl group, which makes the β′-position of the pyrrole ring electron-deficient and destabilizes the transition state **B**.

The assumption of the nucleophilic assistance of the solvent to the cleavage of the C(4)—N bond motivated us to study reactions of THPP with DMAD in protic solvents (methanol, ethanol, aqueous THF, and aqueous dioxane). It turned out that in these solvents, nucleophilic assistance is accompanied by proton migration to the anionic center of the zwitterion, giving 3-alkoxy(hydroxy)alkylpyrroles **30**—**40**.

Compounds **2**, **3**, **5**, **8**, **9**, and **13**—**15** in alcohols transformed into 3-alkoxymethyl- and 3-(2-alkoxy)ethylpyrroles **30**—**35** and **38**—**40**, while compounds **10** and **13** in aqueous dioxane and THF, into 3-hydroxymethylpyrroles **36** and **37** (Scheme 3). Compounds **2**, **3**, **5**, and **8**—**11** with two stereogenic centers were obtained and

Scheme 3



used in reactions as racemic mixtures. The tetrahydropyridine fragment in these THPP exists in the half-chair conformation with *trans*-arrangement of the methyl groups at the C(4) and C(7) atoms.[12] According to NMR data, alkoxy(hydroxy)alkylpyrroles **30**—**36** obtained from compounds **2**, **3**, **5**, and **8**—**11** are mixtures of diastereomers, the diastereomer shown in Scheme 3 being dominant (Tables 2 and 3).

Opening of 2-dimethylaminomethyl-THPP **11** in the reaction with two moles of DMAD in methanol was

Table 2. Chemical shifts in the ^{1}H NMR spectra of 3-alkoxy(hydroxy)alkylpyrroles **30—36**

Compound	Ratio*	δ (*J*/Hz)										
		R^1 (d)	R^2 (s, Me)	R^3	R^4 (s)	R^5	H_α H_β	H_γ (q, *J* = 6.4)	H_δ (s)	CO_2Me (s)	H(4)
30	75	1.28 (*J* = 7.0); 1.46 (*J* = 6.4)	2.60	11.85 (br.s, H)	9.40 (CHO)	1.28 (t, *J* = 7.0)	3.25—3.60 (m)	4.45	4.60	3.91, 3.65	6.95 (d, *J* = 2.8)
	25	1.23 (*J* = 7.0); 1.40 (*J* = 6.4)	2.57	11.90 (br.s, H)	9.40 (CHO)	4.15 (q, *J* = 7.0)			4.65	3.91, 3.65	6.93 (d, *J* = 2.8)
31	80	1.33 (*J* = 7.0); 1.48 (*J* = 6.4)	2.64	10.10 (br.s, H)	—	1.18 (t, Me, *J* =7.0) 3.30—3.60 (m, CH_2)	3.30—3.60 (m)	4.48	4.58	3.92, 3.64	7.18 (q, *J* = 18, *J* = 1.5)
	20	1.30 (*J* = 7.0); 1.43 (*J* = 6.4)	2.69	10.10 (br.s, H)		1.20 (t, Me, *J* = 7.0) 3.30—3.60 (m, CH_2)		4.50	4.58	3.92, 3.64	
32	62	1.29 (*J* = 7.0); 1.42 (*J* = 6.4)	2.65	9.88 (br.s, H)	2.41 (Me)	3.27 (s, Me)	3.35—3.42 (m)	4.37	4.58	3.92, 3.63	6.87 (d, *J* = 2.8)
	38	1.24 (*J* = 7.0); 1.46 (*J* = 6.4)	2.58	9.88 (br.s, H)	2.41 (Me)	3.21 (s, Me)		4.34	4.56	3.91, 3.64	
33	80	1.23 (*J* = 6.4); 1.42 (*J* = 6.4)	2.58	8.11 (br.s, H)	3.30 (MeO)	3.17 (s, Me)	3.10—3.32 (m)	4.30	4.55	3.43, 3.93	6.04 (d, *J* = 2.4)
	20	1.24 (*J* = 6.4); 1.45 (*J* = 6.4)	2.62	8.11 (br.s, H)	4.36 (CH_2)			4.30	4.53	3.43, 3.93	
34	65	1.34 (*J* = 7.0); 1.40 (*J* = 6.4)	2.64	5.30 (d, *J* = 8.2); 5.47 (d, *J* = 15.6); 6.83 (dd, *J* = 8.2, *J* = 15.6)	4.53 (CH_2O)	3.23 (s, Me)	3.25—3.50 (m)	4.41	4.53	3.63, 3.91	6.18 (s)
	35	1.28 (*J* = 7.0); 1.43 (*J* = 6.4)	2.60						4.54	3.63, 3.91	6.19 (s)
35	80	1.34 (*J* = 7.0); 1.40 (*J* = 6.4)	2.64	5.34 (d, *J* =15.3); 5.80 (d, *J* = 8.5); 6.76 (dd, *J* = 15.3, *J* = 7.9)	7.49 (CH=)	3.28 (s, Me)	3.30—3.60 (m)	4.47	4.56	3.65, 3.92	7.68 (s)
	20	1.32 (*J* = 7.0); 1.50 (*J* = 6.4)	2.58					4.45	4.54	3.65, 3.92	7.70 (s)
36	60	1.38 (*J* = 7.6); 1.53 (*J* = 6.4)	2.65	5.25 (d, *J* =15.9); 5.55 (d, *J* =8.5); 7.01 (dd, *J* = 8.5, *J* = 15.9)	9.54 (CHO)	2.10 (br.s, OH)	3.25—3.65 (m)	4.94	4.57	3.91, 3.63	7.10 (s)
	40	1.34 (*J* = 7.6); 1.57 (*J* = 6.4)	2.63		9.53 (CHO)			4.98	4.55	3.91, 3.63	7.08 (s)

* The ratio of the diastereomers.

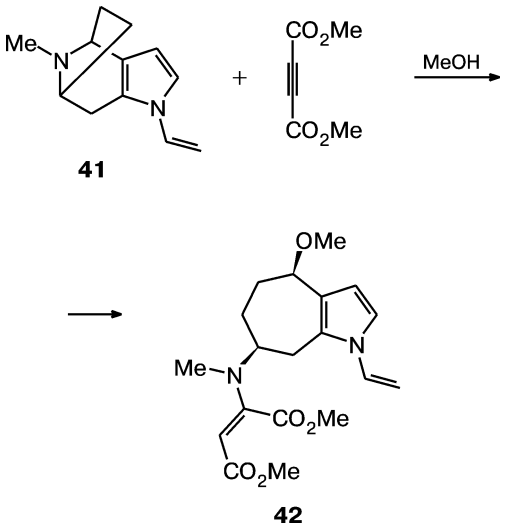
Table 3. Chemical shifts in the ^{1}H NMR spectra of 3-alkoxy(hydroxy)alkylpyrroles **37—40**

Compound	δ (*J*/Hz)								
	R^2	R^3	R^5	H_α	H_β	H_γ (s, CH_2)	H_δ (s)	CO_2Me (s)	H(4)
37	1.14 (t, *J* = 7.0); 3.15 (q, *J* = 7.0)	5.29 (d, *J* =15.3); 5.55 (d, *J* =7.9); 7.10 (dd, *J* = 8.5, *J* = 15.3)	2.41 (br.s, OH)	3.25 (t)	3.15 (t)	4.33	4.70	3.64, 3.92	7.19 (q, *J* = 2.1)
38	4.26 (s, CH_2Ph); 7.22—7.30 (m, H_{arom})	9.50 (br.s, H)	3.30 (s, Me)	3.10—3.30 (m)		4.14	4.77	3.64, 3.96	7.15 (q, (*J* = 2.4)
39	4.25 (s, CH_2Ph); 7.26—7.33 (m, H_{arom})	5.22 (dd, *J* = 8.5, 0.9); 5.30 (dd, *J* = 15.8, *J* = 0.9); 6.97 (dd, *J* = 15.8, *J* = 8.5)	3.38 (s, Me)	2.98—3.01 (m)		4.23	4.83	3.65, 3.93	7.20 (br.s)
40	1.14 (t, *J* = 7.0); 3.30 (q, *J* = 7.0)	5.30 (dd, *J* = 15.9, *J* = 0.9); 5.54 (dd, *J* = 8.2, *J* = 0.9); 7.12 (dd, *J* = 8.2, *J* = 15.9)	3.35 (s, Me)	3.00—3.35 (m)		4.59	4.69	3.64, 3.91	7.21 (q, (*J* = 1.8)

accompanied by elimination of the dimethylamino group, yielding 3-(2-methoxy)ethylpyrrole **33** (ratio of the diastereomers was 1 : 4). A single crystal of the major diastereomer was obtained by crystallization from ethyl acetate. Its molecular structure was determined by X-ray diffraction analysis.[9] According to the crystallographic data, the enamine fragment exists in the *trans*-configuration and the stereogenic centers at the C(2) and C(3) atoms of the pyrrole ring exist in the *R**- and *S**-configuration, respectively. Based on this, we assigned the *trans*-configuration to the enamine fragment in all the 3-vinyl- and 3-alkoxyalkylpyrroles **16**—**23** and **30**—**40** obtained. Analogously, we assigned the *R**- and *S**-configurations to the chiral centers in all major diastereomers **30**—**35**, which are the same configurations as for the corresponding chiral atoms in the starting THPP. Such a stereochemical effect of the opening is probably associated with the ion pair mechanism of this process.

Tricyclic THPP **41** underwent analogous opening under the action of DMAD in methanol to give only one diastereomer **42** in moderate yield (42%) (Scheme 4).

Scheme 4

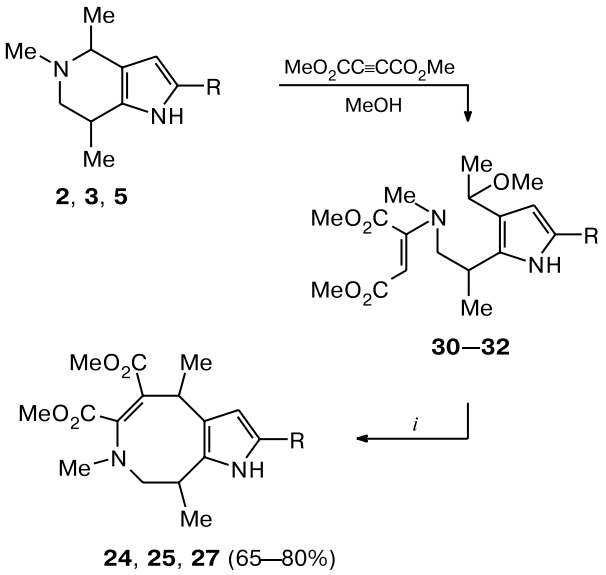


According to $^1H—^1H$ COSY data,[9] compound **42** is a *cis*-isomer with the pseudoaxial methoxy group at the C(4) atom and the pseudoequatorial enamine substituent at the C(7) atom.

Mixtures of the diastereomers of 3-(2-methoxy)ethylpyrroles **30**—**32** in the presence of Lewis acids (boron trifluoride etherate and trimethylsilyl triflate) were converted at 20 °C into tetrahydropyrrolo[2,3-*d*]azocines **24**, **25**, and **27**, respectively (Scheme 5).

The cyclization was stereospecific. Only one isomer of pyrroloazocine with a *cis*-arrangement of the methyl groups in the azocine fragment was isolated, which was identical with that obtained by transformations of the

Scheme 5

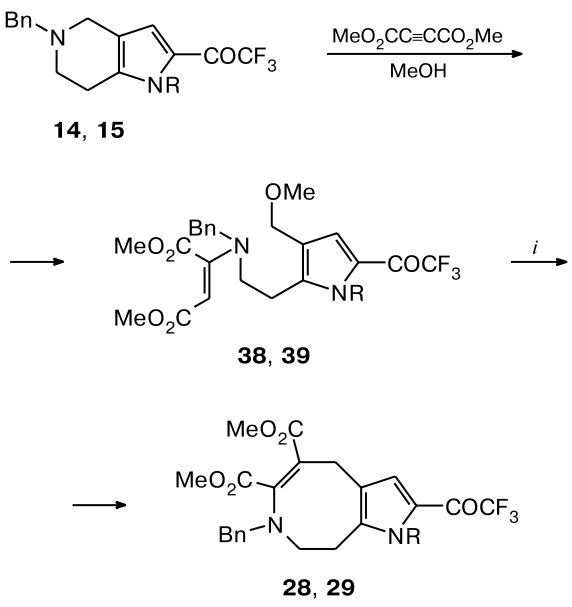


R = CHO (**2**, **24**, **30**), $COCF_3$ (**3**, **25**, **31**), Ac (**5**, **27**, **32**)

i. Lewis acid.

same THPP in polar solvents. The yield in the presence of $BF_3 \cdot Et_2O$ did not exceed 15%; with trimethylsilyl triflate, the yield was 70—80%. Carrying out this process as a "one-pot" reaction, we obtained pyrroloazocines **24**, **25**, and **28** in 65—80% yields over a substantially shorter period of time.

Scheme 6



i. Lewis acid.

An analogous one-pot transformation of N-unsubstituted (in the pyrrole ring) compound **14** at 20 °C in the presence of triflate gave pyrroloazocine **28** in 60% yield. For 1-vinyl-THPP **15**, heating to 50 °C was required at the step of cyclization and the yield of tetrahydropyrroloazocine **29** did not exceed 8%, which is probably due to vinyl polymerization processes (Scheme 6).

Experimental

Mass spectra were recorded on Finnigan MAT 95XL and Hewlett—Packard MS-5988 mass spectrometers (direct inlet probe, ionizing voltage 70 eV). ^{1}H NMR spectra were recorded on Bruker WP-200 and Varian Unity 400 instruments (200 and 400 MHz, respectively) in $CDCl_3$ with Me_4Si as the internal standard. TLC analysis was carried out on Silufol UV-254 plates (spots were visualized in the iodine vapor). For column chromatography, aluminum oxide (Fluka, activity grade II, 60 mesh) and ethyl acetate—hexane (1 : 2—1 : 7) were used.

The yields, physicochemical characteristics, elemental analysis data, and spectroscopic characteristics of the compounds obtained are given in Tables 1—5.

Reactions of THPP with DMAD in aprotic solvents (general procedure). DMAD (1.5 mmol) was added to a solution of THPP (1 mmol) in benzene, acetonitrile, acetone, DMSO, or CS_2 (10 mL). The reaction mixture was stirred at room temperature for 4—24 h. The course of the reactions was monitored by TLC. The solvent was removed *in vacuo*, ether (10 mL) was added, and azocines **24**—**26** and **28** were filtered off. The ether was removed and the residue was chromatographed to give 3-vinylpyrroles **16**—**23** and azocines **24**—**26** and **28**. The physicochemi-

Table 4. Yields and physicochemical characteristics of pyrroloazocines **24**—**29** and 3-alkoxy(hydroxy)alkylpyrroles **30**—**40**

Compound	Yield (%)	M.p./°C (hexane—ethyl acetate)	M^+	Found / Calculated (%)			Molecular formula
				C	H	N	
24	75*	226—228	334	61.13 61.07	6.56 6.63	8.40 8.38	$C_{17}H_{22}N_2O_5$
25	80*	234—236	402	53.88 53.73	5.65 5.26	6.90 6.96	$C_{18}H_{21}F_3N_2O_5$
26	20	236—238	382	62.85 62.82	5.65 5.80	14.43 14.65	$C_{20}H_{22}N_4O_4$
27	68	220—222	348	62.30 62.05	7.03 6.94	8.42 8.04	$C_{18}H_{24}N_2O_5$
28	60*	208—210	450	58.39 58.67	4.72 4.70	6.31 6.22	$C_{22}H_{21}F_3N_2O_5$
29	15	80—82	476	60.25 60.50	4.95 4.83	5.71 5.88	$C_{24}H_{23}F_3N_2O_5$
30	85	Oil	380	59.88 60.00	7.38 7.37	7.37 7.37	$C_{19}H_{28}N_2O_6$
31	76	Oil	448	53.46 53.57	6.01 6.03	6.24 6.25	$C_{20}H_{27}F_3N_2O_6$
32	51	Oil	380	59.80 60.00	7.40 7.37	7.45 7.37	$C_{19}H_{28}N_2O_6$
33	35	108—110	382	59.60 59.68	7.83 7.85	7.32 7.33	$C_{19}H_{30}N_2O_6$
34	49	Oil	394	60.85 60.91	7.38 7.61	7.41 7.11	$C_{20}H_{30}N_2O_6$
35	80	116—117	440	62.95 62.73	6.10 6.36	12.52 12.73	$C_{23}H_{28}N_4O_5$
36	45	Oil	378	60.13 60.32	7.03 6.88	7.21 7.41	$C_{19}H_{26}N_2O_6$
37	33	56—58	432	52.68 52.78	5.31 5.32	6.49 6.48	$C_{19}H_{23}F_3N_2O_6$
38	80	Oil	482	57.19 57.26	5.18 5.19	5.80 5.81	$C_{23}H_{25}F_3N_2O_6$
39	82	70—72	508	59.42 59.06	5.12 5.31	5.82 5.51	$C_{25}H_{27}F_3N_2O_6$
40	44	130—132	446	53.78 53.81	5.53 5.61	6.28 6.28	$C_{20}H_{25}F_3N_2O_6$

* The "one-pot" reaction.

Table 5. Parameters of the ^{1}H NMR spectra of pyrroloazocines **24**—**29**

Compound	δ (*J*/Hz)									
	R^3	R^4 (s)	3-H	4-H	4-R^1 (d, *J* = 7.3)	CO_2Me (s)	R^2	8-H	9-H	9-R^1 (d)
24	10.60 (br.s)	9.30 (CHO)	6.70 (d, *J* = 2.6)	4.52 (q, *J* = 7.3)	1.44	3.68, 3.77	2.68 (s)	3.33 (dd, *J* = 9.0, *J* = 5.6); 3.66—3.68 (m)	3.46 (m)	1.25 (*J* = 6.9)
25	9.96 (br.s)	—	7.01 (d, *J* = 1.5)	4.56 (q, *J* = 7.3)	1.46	3.72, 3.79	2.69 (s)	3.30—3.80 (m)	3.30—3.80 (m)	1.31 (*J* = 6.7)
26	9.35 (br.s)	7.30 ($CH=C(CN)_2$)	6.72 (br.s)	4.52 (q, *J* = 7.3)	1.44	3.72, 3.79	2.69 (s)	3.20—3.75 (m)	3.20—3.75 (m)	1.32 (*J* = 6.7)
27	9.08 (br.s)	2.35 (MeCO)	6.67 (d, *J* = 2.5)	4.50 (q, *J* = 7.3)	1.44	3.71, 3.78	2.67 (s)	3.25—3.70 (m)	3.25—3.70 (m)	1.26 (*J* = 6.7)
28	9.10 (br.s)	—	7.27 (d, *J* = 2.6)	3.79 (s)	—	3.74, 3.76	4.12 (s, CH_2Ph); 6.95—7.05 (m, CHAr); 7.10—7.20 (m)	3.87 (t, *J* = 6.3)	2.90 (t, *J* = 6.3)	—
29	4.75 (dd, *J* = 8.4, *J* = 0.7); 5.10 (dd, *J* = 15.8, *J* = 0.7); 6.35 (dd, *J* = 15.8, *J* = 8.4)	—	6.80 (s)	3.81 (s)	—	3.81, 3.82	4.11 (s, CH_2Ph); 6.90—7.15 (m)	3.92 (t, *J* = 6.5)	2.85 (t, *J* = 6.5)	—

cal constants, ^{1}H and ^{13}C NMR spectra, and mass spectra of vinylpyrroles **16**—**19** and **21**—**23** have been described earlier.[7] The yields, physicochemical characteristics, and elemental analysis data for the azocines obtained are given in Table 4 and their ^{1}H NMR spectra are given in Table 5.

Dimethyl *N*-[2-(5-acetyl-3-vinyl-1*H*-pyrrol-2-yl)propyl]-*N*-methylaminobut-2-enedioate (20). The yield was 81%, m.p. 100—102 °C (hexane—ethyl acetate). Found (%): C, 62.23; H, 6.95; N, 8.20. M^+ = 348. $C_{18}H_{24}N_2O_5$. Calculated (%): C, 62.07; H, 6.90; N, 8.05. *M* = 348. IR, ν/cm^{-1}: 1730 (MeOCO), 1750 (MeOCO), 1680 (MeCO), 1620 ($NCH=CH_2$). ^{1}H NMR, δ: 1.29 (d, 3 H, MeCH, *J* = 7.0 Hz); 2.43 (s, 3 H, MeCO); 2.57 (s, 3 H, NMe); 3.20—3.50 (m, 3 H, NCH_2CH); 3.64, 3.92 (both s, 3 H each, MeO); 4.55 (s, 1 H, $HC(CO_2Me)=$); 5.10 (dd, 1 H, $=CH_2$, *J* = 11.0 Hz, *J* = 1.5 Hz); 5.45 (dd, 1 H, $CH_2=$, *J* = 17.4 Hz, *J* = 1.5 Hz); 6.58 (dd, 1 H, $CH=CH_2$, *J* = 11.0 Hz, *J* = 17.4 Hz); 7.01 (d, 1 H, β-H pyrroles, *J* = 2.4 Hz); 9.88 (br.s, 1 H, NH).

Dimethyl 2-dimethylaminobut-2-enedioate. The yield was 79% (THF), m.p. 83—84 °C (hexane). Found (%): C, 51.67; H, 7.11; N, 7.41. M^+ = 187. $C_8H_{13}NO_4$. Calculated (%): C, 51.33; H, 6.95; N, 7.48. *M* = 187. ^{1}H NMR ($CDCl_3$), δ: 3.05 (s, 6 H), 3.61 (s, 3 H), 3.67 (s, 3 H), 5.02 (s, 1 H). IR, ν/cm^{-1}: 1685, 1710.

Dimethyl 2-morpholinobut-2-enedioate. The yield was 82% (THF), m.p. 92—93 °C (heptane). Found (%): C, 52.33; H, 6.91; N, 6.42. M^+ = 229. $C_{10}H_{15}NO_5$. Calculated (%): C, 52.40; H, 6.55; N, 6.11. *M* = 229. ^{1}H NMR ($CDCl_3$), δ: 3.01—3.12 (m, 4 H), 3.62—3.67 (m, 4 H), 3.69 (s, 3 H), 3.73 (s, 3 H), 4.91 (s, 1 H). IR, ν/cm^{-1}: 1680, 1715.

Reactions of THPP with DMAD in protic solvents (general procedure). DMAD (1.2 mmol; 2.1 mmol in the case of compounds **11** and **12**) was added to a solution of THPP **2**, **3**, **5**, **8**—**15**, and **41** (1 mmol) in methanol, ethanol, aqueous dioxane, and aqueous THF. The reaction mixture was stirred at room temperature for 4—8 h. The course of the reactions was monitored by TLC. The solvents were removed *in vacuo* and the residue was chromatographed. Alkoxy(hydroxy)alkylpyrroles **30**—**42** were eluted as the first fraction. The elemental analysis data and physicochemical constants are given in Table 4; ^{1}H NMR spectra are given in Tables 2 and 3.

Synthesis of tetrahydropyrrolo[2,3-*d*]azocines 24, 25, and 27—29 by the one-pot reaction. DMAD (1.2 mmol) was added to a solution of THPP (1 mmol) in methanol (5 mL). After one day, the solvent was removed *in vacuo* without heating. The residue was dissolved in anhydrous THF (5 mL), trimethylsilyl triflate (1 drop, ~0.05 mmol) was added, and the mixture was left for a day. The solvent was removed *in vacuo*, the residue was treated with aqueous Na_2CO_3, and the product was extracted with ethyl acetate (in the synthesis of azocine **29**, the residue was chromatographed). The yields, physicochemical characteristics, and elemental analysis data for the pyrroloazocines obtained are given in Table 4; their ^{1}H NMR spectra are given in Table 5.

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