NMR Spectroscopic Investigations with Ethyl 1-(Hetero)aryl-5-hydroxy-1*H*-pyrazole-4-carboxylates

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The synthesis of a series of ethyl *N*-1-(hetero)aryl-5-hydroxy-1*H*-pyrazole-4-carboxylates by reaction of diethyl ethoxymethylenemalonate with the appropriate hydrazines is described. According to nmr-spectroscopic investigations (^{1}H- and ^{13}C-nmr) the title compounds exist as 5-hydroxy tautomers in deuteriochloroform as well as in deuteriodimethyl sulfoxide solution.

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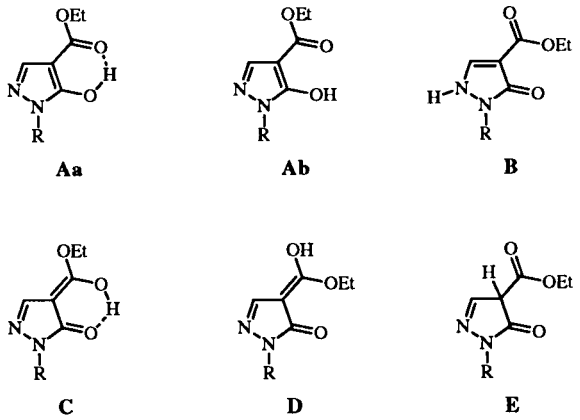
Esters of (N-1-substituted)-5-hydroxypyrazole-4-carboxylic acids - which formally represent pyrazole analogues of salicyclic acid esters - can be assumed to be valuable starting products for the construction of condensed systems or for further functionalization of this azole nucleus. In principle, these compounds can exist in several tautomeric forms (see Scheme 1) [2]. From ir and ^{1}H-nmr spectra it was proposed that ethyl 5-hydroxy-1-phenyl-1*H*-pyrazole-4-carboxylate (**4a**) exists as a pyrazolone (Scheme 1, form **B**) in chlorinated hydrocarbons [3-5]. In contrast, based on ir data, other authors suggested an equilibrium between the chelated (Scheme 1, form **Aa**) and free OH form (Scheme 1, form **Ab**) for this compound [6]. However, with related 4-acyl-5-OH congeners, it was shown that assignments based exclusively on the above methods can lead to incorrect results and that unambiguous determination of tautomeric form(s) is mainly possible by a combination of ^{1}H- and ^{13}C-nmr spectroscopy [7]. In the course of these studies it turned out, that the latter 4-acylpyrazoles are predominantly present in the 5-hydroxy form in deuteriochloroform solution [7,8].

Scheme 1

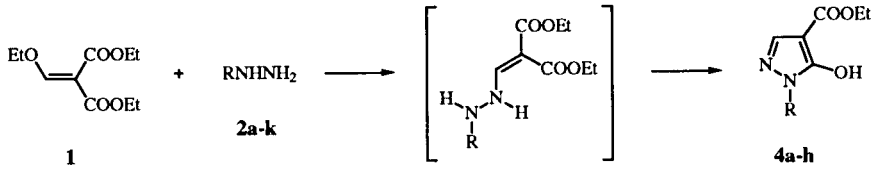


Stimulated by these findings we here report on the synthesis and on systematic ^{1}H- and ^{13}C-nmr investigations of some ethyl 1-aryl- and 1-heteroaryl-5-hydroxypyrazole-4-carboxylates **4** (Scheme 2) in order to assign the structure of such type of compounds in different solvents. Additionally, spectroscopic studies with hydrazino-derivatives of type **3** (which are precursors of the title pyrazole derivatives) are presented.

Synthesis.

The reaction of diethyl ethoxymethylenemalonate (**1**) with the appropriate hydrazines is a well established

Scheme 2



2,3,4	R
a	Ph
b	2-Tolyl
c	3-Tolyl
d	2-Pyridinyl
e	2-Pyrimidinyl
f	2-Quinolinyl

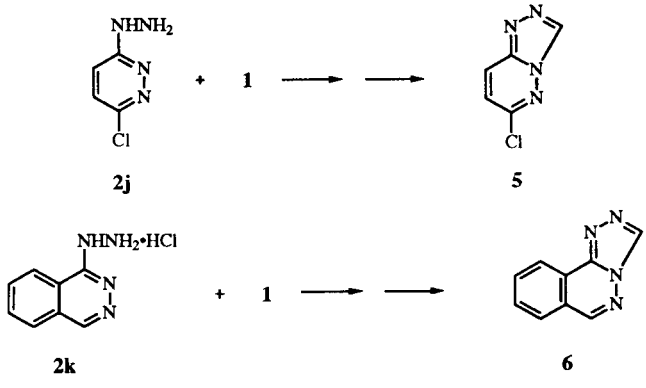
2,3,4	R
g	SO_2Ph
h	Tosyl
i	SO_2-Mesityl
j	6-Chloro-3-pyridazinyl
k	1-Phthalazinyl

method for the synthesis of the desired 5-hydroxypyrazole-4-carboxylates. Dependent upon the reaction conditions the educts are either directly converted into pyrazoles of type **4** (*e.g.* [3,9]) or *via* a two-step process including isolation of the intermediate hydrazino-derivatives **3** [10,11].

Within this study, in cases when the starting hydrazines were used in their hydrochloride form, **2a-c**, the reaction with **1** was carried out by refluxing the educts in excess aqueous potassium carbonate solution directly leading to the pyrazoles **4a-c**. In contrast, the hydrazines **2d-i** were reacted with **1** under neutral conditions (solvent: ethanol) affording the hydrazino derivatives **3d-i**, which after isolation and purification were transformed into the corresponding pyrazoles **3d-h** by heating with potassium carbonate in ethanol. Interestingly, compound **3i** thus could not be converted into **4i**, even application of more drastic reaction conditions (heating to 170° without solvent according to ref [11]) was unsuccessful.

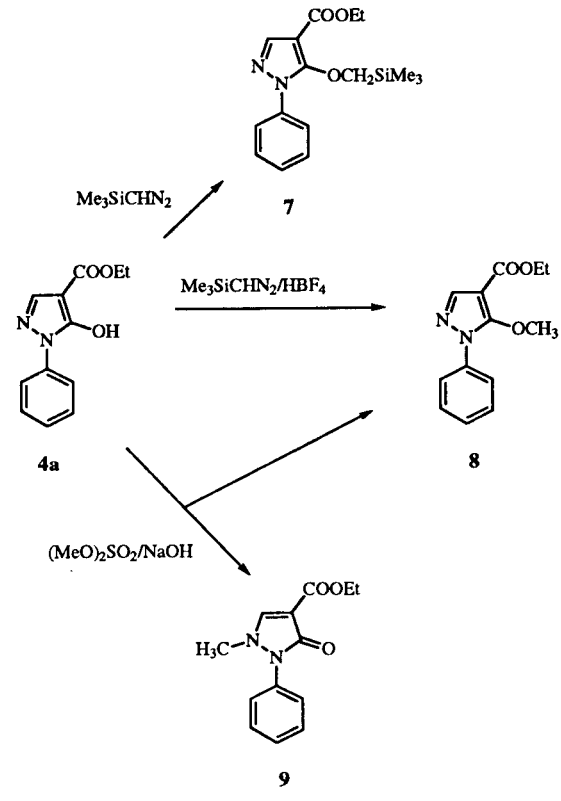
A completely different reaction behavior was found for diazinylhydrazines **2j** and **2k**•HCl (Scheme 3). Heating of **2j** and **1** in dry ethanol did not lead to the corresponding hydrazino compound **3j**, instead the triazolopyridazine **5** was isolated. This is in accordance with the findings of Peet [12] who also proposed a possible reaction mechanism for this case (addition of the azine nitrogen to the activated double bond in intermediate **3j** and subsequent elimination of diethyl malonate). Similarly, reaction of **2k**•HCl with **1** (potassium carbonate/ethanol) afforded the corresponding triazolophthalazine **6**, the formation of which can be considered to follow an analogous mechanism.

Scheme 3



The synthesis of the 5-methoxypyrazole **8** required as model compound was achieved by reaction of **4a** with trimethylsilyldiazomethane in the presence of tetrafluoroboric acid [13], in the absence of the latter reagent the 5-trimethylsilylmethoxy derivative **7** was isolated (Scheme 4). Compound **8** was also obtained together with the *N*-methylpyrazolone **9** upon reaction of **4a** with dimethyl sulfate in aqueous sodium hydroxide solution.

Scheme 4



NMR Spectroscopic Investigations.

Hydrazino Derivatives **3**.

The hydrazino derivatives of type **3** can occur in several tautomeric forms (Scheme 5). On the basis of their ^{1}H-nmr data these compounds can be assumed to exist as tautomers **I** as the =CH-NH-NH- partial structure is evidenced by the occurence of two signals due to exchangeable protons, one of them showing a characteristic vicinal coupling to the alkene-H ($^3J_{=CH,NH}$ ~ 11 Hz) even in deuteriochloroform solution. This is a hint that in the latter solvent there is a considerable contribution of a chelated form (with the (Z)-ester carbonyl O-atom and the =CH-NH-proton involved in an intramolecular hydrogen bond). The ^{13}C-nmr data confirm these findings: the quarternary

Scheme 5

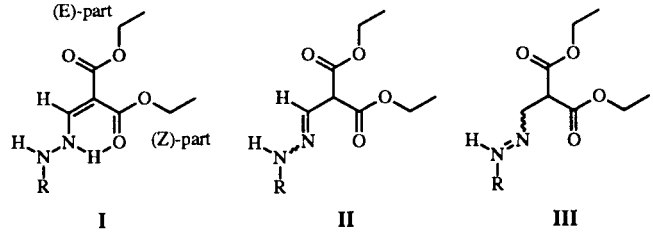


Table 1

^{1}H-NMR Data of Pyrazoles **4a-h**

No.	Solvent	Pyrazole H-3	Ester-H [c] OCH_2	Ester-H [c] CH_3	N1-Substituent	OH [d]
4a	[a]	7.77	4.38	1.40	Ph-H: 7.81 (2,6), 7.47 (3,5), 7.33 (4)	9.6
	[b]	7.82	4.23	1.27	Ph-H: 7.69 (2,6), 7.49 (3,5), 7.34 (4)	11.7
4b	[a]	7.78	4.38	1.40	Ph-H: 7.40-7.25, 2.21 (2-Me)	8.6
4c	[a]	7.76	4.37	1.39	Ph-H: 7.62-7.08, 2.42 (3-Me)	9.3
	[b]	7.79	4.22	1.27	Ph-H: 7.49 (2), 7.47 (6), 7.35 (5), 7.15 (4), 2.34 (3-Me)	11.8
4d	[a]	7.84	4.30	1.34	Pyridine-H: 8.31 (6), 7.92-7.90 (3,4), 7.23 (5)	12.7
	[b]	7.94	4.15	1.23	Pyridine-H: 8.47 (6), 8.12 (4), 7.99 (3), 7.40 (5)	10.0
4e	[a]	7.98	4.34	1.37	Pyrimidine-H: 8.80 (4,6), 7.32 (5) [e]	12.5
4f	[a]	7.95	4.37	1.40	Quinoline-H: 8.39 (4), 8.13 (3), 7.91 (8), 7.88 (5), 7.80 (7), 7.59 (6)	15.2
4g	[a]	7.71	4.33	1.34	Ph-H: 8.09 (2,6), 7.68 (4), 7.56 (3,5)	7.8
	[b]	8.06	4.07	1.16	Ph-H: 7.89 (2,6), 7.77 (4), 7.66 (3,5)	10.7
4h	[a]	7.71	4.31	1.33	Ph-H: 7.96 (2,6), 7.34 (3,5), 2.43 (4-Me)	8.7
	[b]	8.06	4.07	1.16	Ph-H: 7.78 (2,6), 7.45 (3,5), 2.37 (4-Me)	12.9

[a] Deuteriochloroform. [b] Deuteriodimethyl sulfoxide. [c] $^3J(CH_3,OCH_2)$ ~7.1 Hz. [d] The OH-signal is often very broad (2-3 ppm range, particularly in deuteriochloroform solution), the given shift values are the approximative centers of the signal range. [e] ^3J(H4/6,H5) = 4.9 Hz.

alkene-C (C-2) appears as a singlet signal in the gated decoupled spectra ($^2J_{C\text{-}2,=CH}$ <0.4 Hz), whereas the =CH-signal is a double doublet (^1J = 172-174 Hz, $^2J_{=CH,NH}$ ~ 5 Hz). In deuteriochloroform solution, the (*Z*)-ester carbonyl C-atom is shifted 3.2-3.6 ppm downfield compared to the corresponding signal of (*E*)-CO, that can be explained by

Table 2

^{13}C-NMR Chemical Shifts (δ, ppm) and Selected ^{13}C,^{1}H Coupling Constants of Pyrazoles **4a-h**

No.	Solvent	Pyrazole-C C-3	C-4	C-5	Ester-C [c] C=O	OCH_2	CH_3	N1-Substituent	$^nJ(^{13}C,^1H)$ Pyrazole System ^1J(C3,H3)	^2J(C4,H3)	^3J(C5,H3)	Other J
4a	[a]	138.4	95.1	156.6	166.2	60.6	14.3	Ph-C: 137.5 (1), 129.0 (3,5), 127.0 (4), 121.2 (2,6)	191.4	9.5	4.5	—
	[b]	140.2	96.4	154.4	162.4	59.2	14.4	Ph-C: 137.7 (1), 129.0 (3,5), 126.9 (4), 122.2 (2,6)	190.0	8.9	4.8	—
4b	[a]	138.5	94.0	156.8	166.0	60.5	14.3	Ph-C: 135.4, 135.3 (1,2[d]), 131.0, 129.4, 127.2, 126.5 (3,4,5,6 [d]), 17.6 (2-Me)	191.2	9.6	4.8	[e]
4c	[a]	138.3	95.0	156.7	166.3	60.6	14.3	Ph-C: 139.1 (3), 137.5 (1), 128.8 (5), 127.8 (4), 122.0 (2), 118.4 (6), 21.4 (3-Me)	191.3	9.6	4.9	[f]
	[b]	140.0	96.3	154.3	162.4	59.2	14.4	Ph-C: 138.5 (3), 137.6 (1), 128.8 (5), 127.5 (4), 122.8 (2), 119.4 (6), 20.9 (3-Me)	190.0	8.9	4.8	[g]
4d	[a]	142.9	96.9	157.9	162.4	59.8	14.4	Pyr-C: 153.9 (2), 145.0 (6), 140.4 (4), 120.9 (5), 112.8 (3)	190.7	8.9	4.9	—
	[b]	142.6	95.3	158.7	161.8	58.8	14.3	Pyr-C: 150.6 (2), 144.8 (6), 141.6 (4), 121.1 (5), 112.7 (3)	190.0	8.1	5.2	—
4e	[a]	143.9	97.3	157.9	162.1	60.0	14.3	Pyrim-C: 158.3 (4,6), 157.1 (2), 118.6 (5)	192.1	9.1	4.8	[h]
4f	[a]	143.6	97.0	159.0	162.4	59.9	14.5	Quinoline-C: 153.2 (2), 142.7 (8a), 141.0 (4), 131.7 (7), 128.1 (5), 126.8 (6), 126.0 (4a), 125.9 (8), 111.9 (3)	190.6	8.8	4.8	—
4g	[a]	141.2	95.7	159.5	166.0	61.3	14.2	Ph-C: 137.3 (1), 134.9 (4), 129.5 (3,5), 128.4 (2,6)	193.6	9.6	4.8	—
	[b]	145.9	95.3	159.6	161.6	59.1	14.2	Ph-C: 136.7 (1), 134.9 (4), 129.7 (3,5), 127.4 (2,6)	191.3	7.1	5.4	—
4h	[a]	141.1	95.6	159.3	165.3	61.2	14.2	Ph-C: 146.4 (4), 134.3 (1), 130.1 (3,5), 128.4 (2,6), 21.7 (Me)	193.4	9.6	4.8	[i]
	[b]	145.7	95.6	159.4	161.5	59.2	14.2	Ph-C: 145.9 (4), 133.7 (1), 130.1 (3,5), 127.5 (2,6), 21.1 (Me)	191.6	7.8	5.8	[j]

[a] Deuteriochloroform. [b] Deuteriodimethyl sulfoxide. [c] Typical coupling constants (deuteriochloroform): $^3J(CO,OCH_2)$ = 3.3 Hz, $^1J(OCH_2)$ = 148.0 Hz, $^2J(OCH_2,CH_3)$ = 4.4 Hz, $^1J(CH_3)$ = 127.2 Hz, $^2J(CH_3,OCH_2)$ = 2.6 Hz. [d] Unambiguous assignment was not possible. [e] ^1J(Ph-2-CH_3) = 127.9 Hz. [f] ^1J(Ph-3-CH_3) = 126.9 Hz. [g] ^1J(Ph-3-CH_3) = 126.7 Hz. [h] Pyrimidine system: ^1J(C4/6) = 185.6 Hz, ^2J(C4,H5) = 3.3 Hz, ^3J(C4,H6) = 5.5 Hz, ^1J(C5,H5) = 172.2 Hz, ^2J(C5,H4/6) = 7.3 Hz. [i] ^1J(Ph-CH_3) = 127.7 Hz. [j] ^1J(Ph-CH_3) = 127.4 Hz.

deshielding *via* the intramolecular hydrogen bond [14]. The (*Z*)-ester carbonyl C-atom can be independently identified by a ~ 10 Hz vicinal coupling to the alkene-proton (*trans*-position to the alkene proton =CH), whereas the corresponding coupling of (*E*)-CO with =CH is only ~ 4.5 Hz (*cis*-position of the coupled nuclei). Switching to deuteriodimethyl sulfoxide as the solvent leads to an upfield shift for the signals of the =CH-C fragment and those of the ester carbonyl atoms, with the (*Z*)-CO signal being much more affected. This is a hint that in deuteriodimethyl sulfoxide the portion of species with intramolecular hydrogen bond is markedly reduced (or zero).

Pyrazole Derivatives **4**.

The ^{1}H-nmr spectra of pyrazoles **4** (^{1}H-nmr data are collected in Table 1) do not allow an unambiguous assignment of tautomeric forms, only the CH-isomer **E** (Scheme 1) can be excluded. In contrast, ^{13}C-nmr data (Table 2 and Figure 1) lead us to the conclusion that compounds **4** exist as the 5-hydroxy tautomers in deuteriochloroform as well as in deuteriodimethyl sulfoxide solution. This assignment is mainly based on comparison with "fixed" model compounds. Thus, for instance, the ^{13}C nmr data of pyrazole **4a** resemble closely to those of the fixed 5-methoxy derivative **8** or the 5-trimethylsilylmethoxy analogue **7** (Figure 1), whereas comparison with the *N*-methylpyrazolone **9** exhibits marked differences concerning δ (pyrazole C-3) and δ (pyrazole C-5) as well as the chemical shifts of the *N*-phenyl substituent (Ph C-1 and Ph C-2,6). Additionally, opposing **4a** to its des-5-hydroxy congener **10** [15] having an "aromatic" pyrazole system shows similarities of δ (pyrazole C-3) and the ^{13}C chemical shifts of the phenyl rings, the same applies for the pair **4d** and **11** [15] (Figure 1). The above assignment is also confirmed considering the long-range ^{13}C,^{1}H coupling constants on the pyrazole system: in deuteriochloroform solution, for pyrazoles **4a-h** ^{3}J(C5,H3) is 4.5-4.9 Hz, what closely resembles with ^{3}J(C5,H3) = 5.0 Hz for the *O*-methoxy compound **8**, whereas the corresponding coupling constant ^{3}J(C3,H5) in the *N*1-methyl-3-pyrazolone **9** has a value of 7.0 Hz. Also ^{2}J(C4,H3) in **8** (8.9 Hz) is located within the range of ^{2}J(C4,H3) for pyrazoles **4a-h** (8.8-9.6 Hz), whereas the corresponding coupling constant ^{2}J(C4,H5) in **9** is much smaller (4.3 Hz).

A remarkable difference for δ (ester C=O) is found when comparing **4a** (δ = 166.2 ppm) with **7** (δ = 162.2

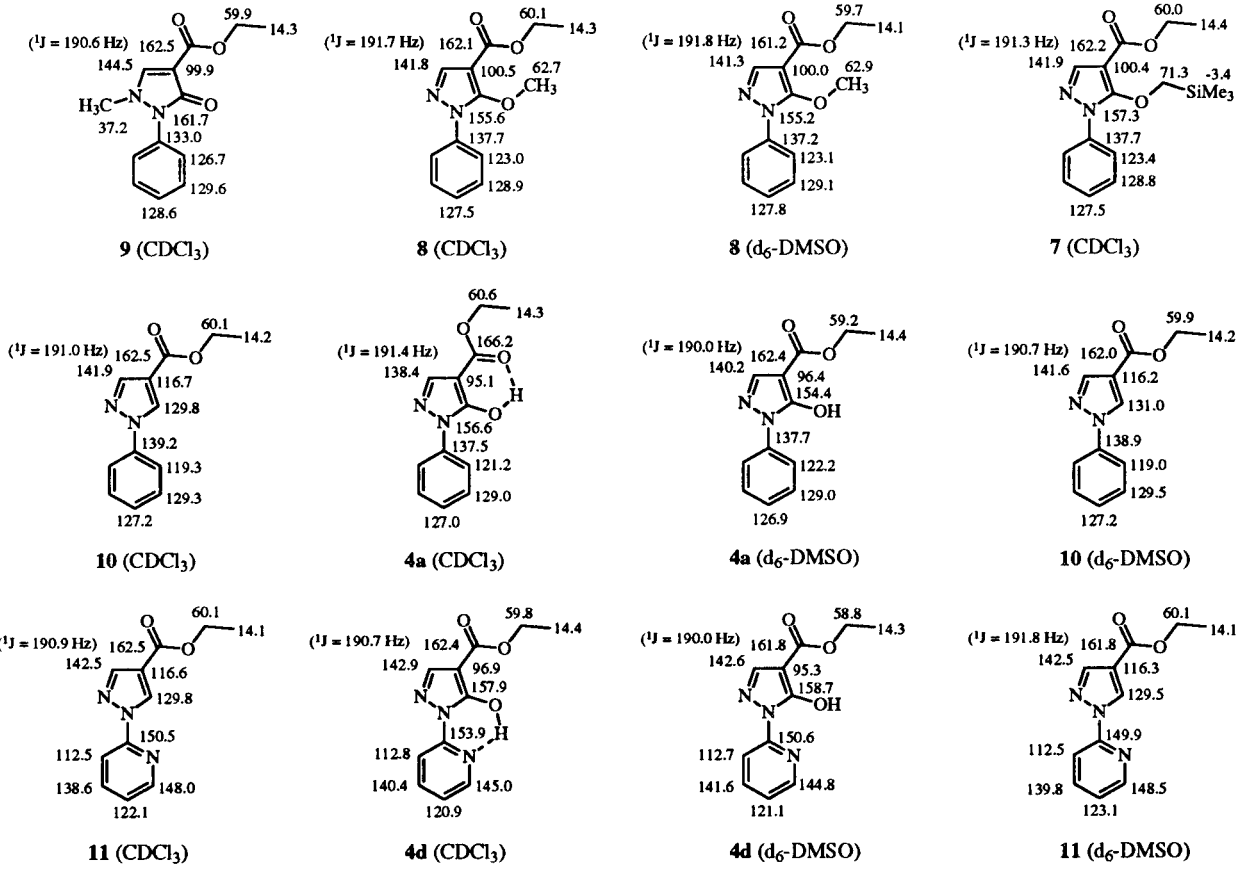


Figure 1. ^{13}C Chemical Shifts of **4a**, **4d** and Related Model Compounds

ppm), **8** (δ = 162.1 ppm) or **10** (δ = 162.5 ppm [15]) in deuteriochloroform solution. However, this phenomenon can be easily explained by the fact that the carbonyl oxygen atom in **4a** is obviously involved in an intramolecular hydrogen bond with the 5-hydroxy proton (Figure 1), which results in a marked downfield shift for the ester carbonyl C-atom [14]. Upon switching to the acceptor deuteriodimethyl sulfoxide as the solvent very similar chemical shifts for C=O of the above compounds were observed (**4a**: 162.4 ppm, **8**: 161.2 ppm, **10**: 162.0 ppm); from this finding the conclusion can be drawn that the mentioned intramolecular hydrogen bond in **4a** is broken in this solvent. The same phenomenon was detected for analogue **4c** as well as for the 1-benzenesulfonyl (**4g**) and the 1-tosyl congener **4h** (Table 2). For *N*-1 heteroaryl derivatives **4d-f**, characterized by a basic nitrogen atom in α-position to the pyrazolyl substituent, a different behaviour was found as with these compounds δ (ester C=O) does not exhibit marked differences between deuteriochloroform and deuteriodimethyl sulfoxide solution and also is nearly identical with that of the corresponding des 5-hydroxy congener (for instance $\delta_{C=O}$ in deuteriochloroform, **4d**: 162.4 ppm, **11**: 162.5 ppm [15]; in deuteriodimethyl sulfoxide, **4d**: 161.8 ppm, **11**: 161.8 ppm). From these observations the conclusion can be drawn that - in contrast to congeners **4a-c** and **4g,h** - with pyrazoles **4d-f** there is no chelation of the ester carbonyl O-atom in deuteriochloroform, instead the 5-OH proton obviously forms a more stable intramolecular hydrogen bond with the basic nitrogen atom of the *N*-1 substituent (Figure 1). Stabilization of 1-(2-pyridinyl)-5-hydroxypyrazoles or 1-(2-quinolinyl)-5-hydroxypyrazoles by such chelation effects have been already described in the literature [2,16].

Conclusively, from our ^{13}C-nmr investigations it emerged that 1-(hetero)aryl-4-ethoxycarbonyl-5-hydroxypyrazoles generally exist as 5-hydroxy tautomers in solution, 1-aryl derivatives are present in a chelated C=O···H-O form (form **Aa** of Scheme 1) in deuteriochloroform solution, switching to deuteriodimethyl sulfoxide as the solvent breaks the intramolecular hydrogen bond (form **Ab**). In contrast, analogues with *N*-1-azinyl or *N*-1-diazinyl substituents having the basic nitrogen atom in α-position to the pyrazolyl moiety are stabilized by an intramolecular hydrogen bond between the 5-OH proton and the (di)azine-*N*-atom (Figure 1, **4d** in deuteriochloroform).

EXPERIMENTAL

Melting points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. The ir spectra were recorded on a Perkin Elmer FTIR 1605 spectrometer, mass spectra were obtained on a Varian MAT 311A or on a Hewlett Packard 5890A/5970B-MSD instrument (both EI, 70 eV). The nmr spectra were recorded on a Varian UnityPlus 300 spectrometer (299.95 MHz for ^{1}H, 75.43 MHz for ^{13}C) at 28°. The solvent signal was used as an internal standard which was related to tetramethylsilane with δ 7.26 ppm and δ 77.0 ppm (^{1}H and ^{13}C in deuteriochloroform) or δ 2.49 ppm and δ 39.5 ppm (^{1}H and ^{13}C in deuteriodimethyl sulfoxide). Unambiguous assignments were achieved on the basis of coupling information (^{13}C: gated decoupled spectra), *via* HMQC-experiments [17] as well as relying on 1D-HETCOR [18] and 1D- or 2D-long-range INEPT spectra [19] with selective DANTE-excitation. The digital resolution was 0.25 Hz/data point for ^{1}H-nmr spectra, 0.55 Hz/data point for broad-band decoupled ^{13}C-nmr spectra and 0.29 Hz/data point for ^{1}H-coupled ^{13}C-nmr spectra. Column chromatographic separations were performed on Merck Kieselgel 60 (70-230 mesh). Yields given below are not optimized. All educts except hydrazines **2e** [20], **2f** [21] and **2j** [22] are commercially available.

General Procedure for the Preparation of the Hydrazino Derivatives **3e-3i**.

A solution of one equivalent of diethyl ethoxymethylenemalonate (**1**) and one equivalent of the appropriate hydrazine **2** in a minimum amount of dry ethanol was heated to reflux until tlc-monitoring showed completion of the reaction (~ 1-3 hours). Cooling to room temperature led to crystallization of the hydrazino derivatives **3** (except **3f**), which were collected by filtration and purified by recrystallization.

Diethyl [[2-(2-Pyridinyl)hydrazino]methylene]propanedicarboxylate (**3d**) [11].

Compound **3d** had ^{1}H-nmr (deuteriochloroform): δ 10.04 (d, J = 11.1 Hz, 1H, NH), 8.16 (d, J = 11.1 Hz, 1H, =CH), 8.15 (m, 1H, pyridine H-6), 7.75 (s, 1H, Pyr-NH), 7.57 (m, 1H, pyridine H-4), 6.82 (m, 1H, pyridine H-5), 6.70 (m, 1H, pyridine H-3), 4.26 (q, J = 7.1 Hz, 2H, (*Z*)-OCH_2), 4.17 (q, J = 7.1 Hz, 2H, (*E*)-OCH_2), 1.33 (t, J = 7.1 Hz, 3H, (*Z*)-CH_3), 1.25 (t, J = 7.1 Hz, 3H, (*E*)-CH_3); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 10.26 (d, J = 12.1 Hz, NH), 9.22 (s, 1H, Pyr-NH), 8.12 (m, 1H, pyridine H-6), 7.96 (d, J = 12.1 Hz, 1H, =CH), 7.60 (m, 1H, pyridine H-4), 6.81 (m, 1H, pyridine H-5), 6.64 (m, 1H, pyridine H-3), 4.15 (q, 2H, OCH_2), 4.07 (q, 2H, OCH_2), 1.22 (t, 3H, CH_3), 1.17 (t, 3H, CH_3); ^{13}C-nmr (deuteriochloroform): δ 168.7 ((*Z*)-C=O), 165.1 ((*E*)-C=O), 161.4 (=CH), 159.1 (pyridine C-2), 148.2 (pyridine C-6), 138.4 (pyridine C-4), 117.0 (pyridine C-5), 106.8 (pyridine C-3), 91.9 (C-2), 60.2 ((*Z*)-OCH_2), 59.8 ((*E*)-OCH_2), 14.3 ((*E*)-CH_3), 14.2 ((*Z*)-CH_3); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 166.9 ((*Z*)-C=O), 164.6 ((*E*)-C=O), 159.6 (=CH), 158.5 (pyridine C-2), 147.6 (pyridine C-6), 137.8 (pyridine C-4), 115.9 (pyridine C-5), 107.4 (pyridine C-3), 88.6 (C-2), 59.1 and 59.0 (OCH_2), 14.3 (CH_3).

Diethyl [[2-(2-Pyrimidinyl)hydrazino]methylene]propanedicarboxylate (**3e**).

Recrystallization from isopropanol afforded a 57% yield of colorless crystals of mp 136-137°; ^{1}H-nmr (deuteriochloroform): δ 10.17 (d, J = 11.5 Hz, 1H, NH), 8.39 (d, ^{3}J = 4.9 Hz, 2H, pyrimidine H-4,6), 8.25 (s, 1H, Het-NH), 8.11 (d, J = 11.5 Hz, 1H, =CH), 6.77 (t, ^{3}J = 4.9 Hz, 1H, pyrimidine H-5), 4.26 (q, J = 7.1 Hz, 2H, (*Z*)-OCH_2), 4.16 (q, J = 7.1 Hz, 2H, (*E*)-OCH_2), 1.32 (t, J = 7.1 Hz, 3H, (*Z*)-CH_3), 1.24 (t, J = 7.1 Hz, 3H, (*E*)-CH_3); ^{13}C-nmr (deuteriochloroform): δ 168.6 ((*Z*)-C=O,

$^3J_{CO,=CH}$ = 10.3 Hz, $^3J_{CO,OCH2}$ = 3.1 Hz), 165.2 ((*E*)-C=O, $^3J_{CO,=CH}$ = 4.3 Hz, $^3J_{CO,OCH2}$ = 3.1 Hz), 162.5 (pyrimidine C-2, $^3J_{C2,H4/6}$ = 11.7 Hz), 160.8 (=CH, ^1J = 171.9 Hz, $J_{=CH,NH}$ = 5.2 Hz), 158.4 (pyrimidine C-4/6, ^1J = 180.8 Hz, $^2J_{C4/6,H5}$ = 3.4 Hz, $^3J_{C4,H6}$ = 5.6 Hz), 114.2 (pyrimidine C-5, ^1J = 169.8 Hz, $^2J_{C5,H4/6}$ = 7.4 Hz), 91.8 (C-2), 60.2 ((*Z*)-OCH_2, ^1J = 147.2 Hz, ^2J = 4.3 Hz), 59.8 ((*E*)-OCH_2, ^1J = 147.0 Hz, ^2J = 4.5 Hz), 14.3 ((*E*)-CH_3, ^1J = 126.7 Hz, ^2J = 2.5 Hz), 14.2 ((*Z*)-CH_3, ^1J = 127.0 Hz, ^2J = 2.5 Hz); ir: cm^{-1} 3272, 3213 (N-H), 1713, 1660 (C=O); ms: (130°) m/z (%) 280 (M^+, 9), 234 (20), 189 (13), 188 (34), 121 (51), 120 (12), 96 (13), 95 (100), 68 (24), 43 (8).

Anal. Calcd. for $C_{12}H_{16}N_4O_4$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.64; H, 5,47; N, 20.20.

Diethyl [[2-(2-Quinolinyl)hydrazino]methylene]propanedicarboxylate (**3f**).

The reaction mixture was evaporated *in vacuo* and the oily residue, which solidified with standing, was then recrystallized from aqueous ethanol to give a 92% yield of yellow crystals with mp 119°; ^{1}H-nmr (deuteriochloroform): δ 10.28 (broad s, 1H, NH), 8.22 (broad s, 1H, =CH), 8.01 (m, 1H, quinoline H-4), 7.74-7.26 (m, 5H, quinoline H-5,6,7,8 and quinoline-NH), 6.94 (m, 1H, quinoline H-3), 4.31 (q, J = 7.2 Hz, 2H, (*Z*)-OCH_2), 4.23 (q, J = 7.2 Hz, 2H, (*E*)-OCH_2), 1.38 (t, J = 7.2 Hz, 3H, (*Z*)-CH_3), 1.29 (t, J = 7.2 Hz, 3H, (*E*)-CH_3); ^{13}C-nmr (deuteriochloroform): δ 168.8 ((*Z*)-C=O), 166.6 (quinoline C-2), 165.2 ((*E*)-C=O), 160.3 (=CH), 138.5 (quinoline C-4), 130.3, 129.9, 127.6, 124.8, 123.8, 123.2 (quinoline C-4a,5,6,7,8,8a; not unequivocally assigned), 114.7 (quinoline C-3), 91.8 (C-2), 60.2 ((*Z*)-OCH_2), 59.9 ((*E*)-OCH_2), 14.3 (CH_3); ir: cm^{-1} 3263 (N-H), 1687, 1646 (C=O); ms: (140°) m/z (%) 329 (M^+, 4), 238 (11), 171 (13), 170 (100), 169 (17), 144 (19), 142 (11), 133 (13), 128 (12), 116 (16), 115 (35), 88 (11), 45 (19), 43 (27), 42 (12).

Anal. Calcd. for $C_{17}H_{19}N_3O_4$: C, 62.00; H, 5.81; N, 12.76. Found: C, 61.85; H, 5.51; N, 12.48.

Diethyl [(2-Benzenesulfonylhydrazino)methylene]propanedicarboxylate (**3g**).

The precipitated crystals were combined with material obtained upon concentration of the filtrate. Recrystallization from ethanol yielded 75% of colorless crystals, mp 160-161°; ^{1}H-nmr (deuteriochloroform): δ 9.69 (d, J = 11.0 Hz, 1H, NH), 7.87 (m, 2H, Ph H-2,6), 7.84 (d, J = 11.0 Hz, 1H, =CH), 7.66 (m, 1H, Ph H-4), 7.55 (m, 2H, Ph H-3,5), 4.19 (q, J = 7.1 Hz, 2H, (*Z*)-OCH_2), 4.12 (q, J = 7.1 Hz, 2H, (*E*)-OCH_2), 1.28 (t, J = 7.1 Hz, 3H, (*Z*)-CH_3), 1.23 (t, J = 7.1 Hz, 3H, (*E*)-CH_3); ^{13}C-nmr (deuteriochloroform): δ 168.0 ((*Z*)-C=O, $^3J_{CO,=CH}$ = 10.1 Hz, $^3J_{CO,OCH2}$ = 3.3 Hz), 164.6 ((*E*)-C=O, $^3J_{CO,=CH}$ = 4.5 Hz, $^3J_{CO,OCH2}$ = 3.0 Hz), 159.8 (=CH, ^1J = 174.0 Hz, $J_{=CH,NH}$ = 4.8 Hz), 136.5 (Ph C-1), 134.1 (Ph C-4, ^1J = 162.7 Hz), 129.4 (Ph C-3,5), 128.3 (Ph C-2,6), 93.9 (C-2), 60.5 ((*Z*)-OCH_2, ^1J = 147.6 Hz, ^2J = 4.5 Hz), 60.1 ((*E*)-OCH_2, ^1J = 147.1 Hz, ^2J = 4.0 Hz), 14.2 (CH_3, ^1J = 126.9 Hz, ^2J = 2.5 Hz), 14.15 (CH_3, ^1J = 126.9 Hz, ^2J = 2.5 Hz); ir: cm^{-1} 3350 (N-H), 1719 (C=O); ms: (180°) m/z (%) 342 (M^+, 27), 297 (19), 251 (15), 201 (82), 155 (19), 143 (10), 142 (14), 141 (78), 128 (22), 127 (100), 125 (12), 111 (19), 110 (76), 99 (96), 83 (12), 78 (23), 77 (89), 73 (15), 71 (29), 55 (30), 53 (19), 51 (15), 46 (10), 45 (29), 43 (19).

Anal. Calcd. for $C_{14}H_{18}N_2O_6S$: C, 49.11; H, 5.30; N, 8.18. Found: C, 48.96; H, 5.12; N, 8.12.

Diethyl [[2-(4-Methylbenzenesulfonyl)hydrazino]methylene]propanedicarboxylate (**3h**).

Recrystallization from ethanol afforded a 68% yield of colorless crystals, mp 163-164°; ^{1}H-nmr (deuteriochloroform): δ 9.70 (d, J = 11.0 Hz, 1H, NH), 7.84 (d, J = 11.0 Hz, 1H, =CH), 7.74 (m, 2H, Ph H-2,6), 7.36 (m, 2H, Ph H-3,5), 7.12 (s, 1H, SO_2NH), 4.21 (q, J = 7.1 Hz, 2H, (*Z*)-OCH_2), 4.13 (q, J = 7.1 Hz, 2H, (*E*)-OCH_2), 2.45 (s, 3H, Tos CH_3), 1.30 (t, J = 7.1 Hz, 3H, (*Z*)-CH_3), 1.24 (t, J = 7.1 Hz, 3H, (*E*)-CH_3); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 10.34 (s, 1H, SO_2NH), 9.73 (d, J = 11.5 Hz, 1H, NH), 7.67 (m, 2H, Ph H-2,6), 7.62 (d, J = 11.5 Hz, =CH), 7.46 (m, 2H, Ph H-3,5), 4.07 (q, J = 7.1 Hz, 2H, OCH_2), 4.00 (q, J = 7.1 Hz, 2H, OCH_2), 2.40 (s, 3H, Tos CH_3), 1.15 (t, J = 7.1 Hz, 3H, ester CH_3), 1.13 (t, J = 7.1 Hz, 3H, ester CH_3); ^{13}C-nmr (deuteriochloroform): δ 168.1 ((*Z*)-C=O), 164.6 ((*E*)-C=O), 159.8 (=CH), 145.5 (Ph C-4), 133.2 (Ph C-1), 130.2 (Ph C-3,5), 128.4 (Ph C-2,6), 94.1 (C-2), 60.6 ((*Z*)-OCH_2), 60.1 ((*E*)-OCH_2), 21.6 (Tos CH_3), 14.22 and 14.17 (ester CH_3); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 166.4 ((*Z*)-C=O, $^3J_{CO,=CH}$ = 10.2 Hz, $^3J_{CO,OCH2}$ = 3.2 Hz), 163.9 ((*E*)-C=O, $^3J_{CO,=CH}$ = 4.1 Hz), 158.8 (=CH, ^1J = 172.2 Hz, $J_{=CH,NH}$ = 5.9 Hz), 144.5 (Ph C-4), 133.7 (Ph C-1), 129.9 (Ph C-3,5), 127.9 (Ph C-2,6), 91.5 (C-2), 59.6 and 59.3 (OCH_2), 21.0 (Tos CH_3, ^1J = 127.3 Hz, ^3J = 4.3 Hz), 14.1 and 14.0 (ester CH_3); ir: cm^{-1} 3347 (N-H), 1720 (C=O); ms: (160°) m/z (%) 356 (M^+, 9), 201 (36), 200 (11), 156 (11), 155 (59), 128 (17), 127 (100), 110 (22), 99 (79), 92 (23), 91 (87), 77 (11), 71 (21), 65 (22), 55 (24), 53 (15), 45 (18), 44 (17), 43 (14).

Anal. Calcd. for $C_{15}H_{20}N_2O_6S$: C, 50.55; H, 5.66; N, 7.86. Found: C, 50.57; H, 5.38; N, 7.81.

Diethyl [[2-(2,4,6-Trimethylbenzenesulfonyl)hydrazino]methylene]propanedicarboxylate (**3i**).

The precipitated crystals were combined with material obtained upon concentration of the filtrate. Recrystallization from ethanol afforded 65% of colorless crystals of mp 154-155°; ^{1}H-nmr (deuteriochloroform): δ 9.74 (d, J = 11.1 Hz, 1H, NH), 7.59 (d, J = 11.1 Hz, 1H, =CH), 7.19 (s, 1H, SO_2NH), 6.96 (s, 2H, Ph H-3,5), 4.20 (q, J = 7.1 Hz, 2H, (*Z*)-OCH_2), 4.07 (q, J = 7.1 Hz, 2H, (*E*)-OCH_2), 2.58 (s, 6H, Ph-2,6-CH_3), 2.29 (s, 3H, Ph-4-CH_3), 1.28 (t, J = 7.1 Hz, 3H, (*Z*)-ester CH_3), 1.19 (t, J = 7.1 Hz, 3H, (*E*)-ester CH_3); ^{13}C-nmr (deuteriochloroform): δ 167.8 ((*Z*)-C=O, $^3J_{CO,=CH}$ = 10.3 Hz, $^3J_{CO,OCH2}$ = 3.4 Hz), 164.6 ((*E*)-C=O, $^3J_{CO,=CH}$ = 4.5 Hz, $^3J_{CO,OCH2}$ = 3.1 Hz), 159.6 (=CH, ^1J = 173.9 Hz, ^2J and ^3J = 5.4 and 2.5 Hz), 144.1 (Ph C-4, $^2J_{C4,Me}$ = 5.8 Hz), 141.1 (Ph C-2,6, $^2J_{C2/6,Me}$ = 5.8 Hz), 132.2 (Ph C-3,5, ^1J = 159.5 Hz), 129.7 (Ph C-1), 93.6 (C-2), 60.5 ((*Z*)-OCH_2, ^1J = 147.7 Hz, ^2J = 4.5 Hz), 60.0 ((*E*)-OCH_2, ^1J = 147.2 Hz, ^2J = 4.5 Hz), 22.8 (Ph-2,6-CH_3, ^1J = 129.3 Hz), 20.9 (Ph-4-CH_3, ^1J = 127.3 Hz, ^3J = 4.7 Hz), 14.13 ((*Z*)-ester CH_3, ^1J = 127.1 Hz, ^2J = 2.7 Hz), 14.11 ((*E*)-ester CH_3, ^1J = 126.8 Hz, ^2J = 2.7 Hz); ir: cm^{-1} 3184 (N-H), 1692, 1666 (C=O): ms: (140°) m/z (%) 384 (M^+, 5), 201 (40), 155 (24), 145 (10), 128 (24), 127 (100), 120 (25), 119 (79), 117 (10), 110 (11), 99 (26).

Anal. Calcd. for $C_{17}H_{24}N_2O_6S$: C, 53.11; H, 6.29; N, 7.29. Found: C, 52.97; H, 6.00; N, 7.28.

General Procedure for the Preparation of Pyrazoles **4** from Diethyl Ethoxymethylenemalonate (**1**) and substituted Hydrazines **3**.

To a mixture of 1 mmole of the hydrazine hydrochloride and

276 mg (2 mmoles) of potassium carbonate in 5 ml of water were added 216 mg (1 mmole) of diethyl ethoxymethylenemalonate (**1**). The resulting mixture was heated to reflux for 2 hours, after cooling it was extracted with two 5 ml portions of ethyl acetate and the remaining aqueous phase was then acidified to *p*H 2 with 2*N* hydrochloric acid. After repeated extraction with ethyl acetate the combined organic phases were dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo*.

Ethyl 5-Hydroxy-1-(2-methylphenyl)-1*H*-pyrazole-4-carboxylate (**4b**).

The residue consisted of an oil which solidified with standing affording 197 mg (80%) of a yellowish solid with mp 86-87°; ir: cm^{-1} 2538, 1720 (C=O), 1688 (C=O); ms: m/z (%) 246 (M^+, 60), 201 (22), 200 (100), 183 (29), 173 (28), 172 (54), 171 (15), 144 (13), 117 (19), 105 (11), 104 (16), 91 (23), 77 (12), 65 (14).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.18; H, 5.43; N, 11.09.

Ethyl 5-Hydroxy-1-(3-methylphenyl)-1*H*-pyrazole-4-carboxylate (**4c**).

The residue was recrystallized from aqueous ethanol to give 127 mg (52%) of yellowish needles, mp 87-89°; ir: cm^{-1} 2905, 2773, 1710 (C=O); ms: (100°) m/z (%) 247 (M^++1, 14), 246 (M^+, 72), 201 (69), 200 (100), 132 (65), 106 (16), 105 (82), 104 (27), 91 (60), 79 (12), 78 (13), 77 (16), 65 (27).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.43; H, 5.53; N, 11.15.

General Procedure for the Preparation of Pyrazoles **4** from the Hydrazino Derivatives **3**.

A mixture of 1 mmole of the hydrazino derivative **3** and 138 mg (1 mmole) of potassium carbonate in 10 ml of dry ethanol was refluxed until tlc-monitoring showed completion of the reaction (1-6 hours). The residue obtained after evaporation of ethanol was taken up in a 1:1 mixture of dichloromethane and water (20 ml), the aqueous phase was separated and acidified to *p*H 4 with 2*N* hydrochloric acid. After repeated extraction with dichloromethane the combined dichloromethane phases were dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo*. The residue was recrystallized from an appropriate solvent.

Ethyl 5-Hydroxy-1-(2-pyridinyl)-1*H*-pyrazole-4-carboxylate (**4d**) [11].

Compound **4d** had ir: cm^{-1} 1685 (C=O), 1620.

Ethyl 5-Hydroxy-1-(2-pyrimidinyl)-1*H*-pyrazole-4-carboxylate (**4e**).

Recrystallization from 2-propanol gave 170 mg (73%) of yellowish needles with mp 156° (lit [23] mp 155-158°); ir: cm^{-1} 1706 (C=O), 1622.

Ethyl 5-Hydroxy-1-(2-quinolinyl)-1*H*-pyrazole-4-carboxylate (**4f**).

Recrystallization from 2-propanol afforded 156 mg (55%) of yellow crystals with mp 142-143°; ir: cm^{-1} 1718 (C=O), 1618; ms: (150°) m/z (%) 284 (M^++1, 30), 283 (M^+, 100), 239 (22), 238 (98), 237 (84), 212 (10), 211 (72), 210 (43), 209 (17), 171 (17), 170 (78), 169 (32), 144 (19), 143 (34), 142 (20), 129 (38), 128 (45), 116 (22), 102 (17), 101 (15), 77 (9), 45 (9).

Anal. Calcd. for $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.63; N, 14.83. Found: C, 63.79; H, 4.77; 14.71.

Ethyl 1-Benzenesulfonyl-5-hydroxy-1*H*-pyrazole-4-carboxylate (**4g**).

Recrystallization from ethanol afforded 189 mg (64%) of colorless crystals, mp 135-136°; ir: cm^{-1} 1718 (C=O), 1654; ms: (130°) m/z (%) 296 (M^+, 7), 188 (12), 186 (25), 141 (46), 111 (11), 110 (45), 78 (14), 77 (100), 71 (10), 53 (18), 51 (17).

Anal. Calcd. for $C_{12}H_{12}N_2O_5S$: C, 48.64; H, 4.08; N, 9.45. Found: C, 48.87; H, 4.07; N, 9.46.

Ethyl 5-Hydroxy-1-(4-methylbenzenesulfonyl)-1*H*-pyrazole-4-carboxylate (**4h**).

Recrystallization from ethanol afforded 208 mg (67%) of colorless crystals, mp 164-165°; ir: cm^{-1} 1718 (C=O), 1668; ms: (160°) m/z (%) 310 (M^+, 3), 246 (14), 200 (15), 174 (11), 155 (54), 110 (21), 92 (14), 91 (100), 77 (10), 65 (22), 53 (12).

Anal. Calcd. for $C_{13}H_{14}N_2O_5S$: C, 50.32; H, 4.55; N, 9.03. Found: C, 50.50; H, 4.49; N, 9.10.

6-Chloro-[1,2,4]triazolo[4,3-*b*]pyridazine (**5**).

A solution of 506 mg (3.5 mmoles) of 6-chloro-3-hydrazinopyridazine (**2j**) and 757 mg (3.5 mmoles) of **1** in 15 ml of dry ethanol was heated to reflux for 1 hour. After cooling, the precipitate (216 mg) was filtered off and and the remaining solution was concentrated to afford another 193 mg of material. The combined products were recrystallized from isopropanol to yield 375 mg (69%) of **5** as colorless needles of mp 204-205° (lit [24] mp 203.5°, lit [12] mp 202-203°); ^{1}H-nmr (deuteriochloroform): δ 9.03 (d, ^5J = 0.7 Hz, 1H, triazolo H-5), 8.10 (dd, ^3J = 9.5 Hz, ^5J = 0.7 Hz, 1H, pyridazine H-4), 7.13 (d, ^3J = 9.5 Hz, 1H, pyridazine H-5); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 9.61 (d, ^5J = 0.7 Hz, 1H, triazolo H-5), 8.43 (dd, ^3J = 9.5 Hz, ^5J = 0.7 Hz, 1H, pyridazine H-4), 7.46 (d, ^3J = 9.5 Hz, 1H, pyridazine H-5); ^{13}C-nmr (deuteriochloroform): δ 149.8 (pyridazine C-6), 138.4 (triazolo C-5, ^1J = 219.5 Hz), 126.2 (pyridazine C-4, ^1J = 176.3 Hz), 122.7 (pyridazine C-5, ^1J = 177.7 Hz); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 149.0 (pyridazine C-6, $^3J_{C6,H4}$ = 11.5 Hz), 142.1 (pyridazine C-3), 138.7 (triazolo C-5, ^1J = 221.0 Hz), 126.5 (pyridazine C-4, ^1J = 178.3 Hz), 122.9 (pyridazine C-5, ^1J = 180.2 Hz).

[1,2,4]Triazolo[3,4-*a*]phthalazine (**6**).

To a solution of 787 mg (4 mmoles) of 1-hydrazinophthalazine hydrochloride (**2k•HCl**) and 1.106 g (8 mmoles) of potassium carbonate in 30 ml of dry ethanol were added 865 mg (4 mmoles) of **1** and the resulting mixture was heated to reflux for 3.5 hours. After removing the solvent *in vacuo* the residue was repeatedly extracted with ethyl acetate, the combined extracts were evaporated and the residue was purified by column chromatography (eluent: ethyl acetate) followed by recrystallization from water to afford 354 mg (52%) of colorless needles of mp 190-191° (lit [25] mp 190-191°, lit [26] mp 193-194°); ^{1}H-nmr (deuteriochloroform): δ 8.99 (s, 1H, triazolo H-5), 8.61 (d, 1H, phthalazine H-8), 8.60 (s, 1H, phthalazine H-4), 7.95-7.88 (m, 2H, phthalazine H-7, phthalazine H-5), 7.78 (m, 1H, phthalazine H-6); ^{13}C-nmr (deuteriochloroform): δ 148.0 (phthalazine C-4, ^1J = 184.1 Hz, $^3J_{C4,H5}$ = 5.2 Hz), 142.4 (phthalazine C-1), 139.5 (triazolo C-5, ^1J = 217.0 Hz), 134.0 (phthalazine C-7, ^1J = 163.3 Hz, $^3J_{C7,H5}$ = 7.6 Hz), 130.8 (phthalazine C-6, ^1J = 164.5 Hz, $^3J_{C6,H8}$ = 8.0 Hz), 128.0 (phthalazine C-5, ^1J = 163.3 Hz), 123.4 and 123.3 (phthalazine C-4a, C-8a), 123.2 (phthalazine C-8, ^1J = 166.9 Hz, $^3J_{C8,H6}$ = 7.2 Hz); ms: m/z (%) 171 (M^++1, 50), 170

(M^+, 100), 130 (12), 116 (15), 115 (81), 114 (51), 89 (14), 88 (62), 87 (14), 76 (12), 64 (12), 63 (20), 62 (36), 58 (15), 51 (11).

Ethyl 1-Phenyl-5-trimethylsilylmethoxy-1*H*-pyrazole-4-carboxylate (**7**).

To a stirred solution of 232 mg (1 mmole) of **4a** in 2 ml of dioxane was successively added 1 ml (2 mmoles) of a 2*M* solution of trimethylsilyldiazomethane in *n*-hexane at ambient temperature. After the evolution of nitrogen had ceased stirring was continued for 8 hours, then the solvent was removed *in vacuo* and the remaining oil was subjected to preparative tlc (eluent: dichloromethane). Extraction with ethyl acetate and evaporation of the combined extracts gave 204 mg (64%) of a yellowish oil; ^{1}H-nmr (deuteriochloroform): δ 7.92 (s, 1H, pyrazole H-3), 7.63 (m, 2H, Ph H-2,6), 7.44 (m, 2H, Ph H-3,5), 7.34 (m, 1H, Ph H-4), 4.32 (q, J = 7.1 Hz, 2H, ester OCH_2), 4.13 (s, 2H, OCH_2Si), 1.37 (t, J = 7.1 Hz, 3H, ester CH_3), 0.02 (s, 9H, $SiMe_3$); ^{13}C-nmr (deuteriochloroform): δ 162.2 (C=O, $^3J_{CO,OCH2}$ = 3.3 Hz), 157.3 (pyrazole C-5, $^3J_{C5,H3}$ = 4.8 Hz, $^3J_{C5,OCH2Si}$ = 2.4 Hz), 141.9 (pyrazole C-3, ^1J = 191.3 Hz), 137.7 (Ph C-1), 128.8 (Ph C-3,5), 127.5 (Ph C-4), 123.4 (Ph C-2,6), 100.4 (pyrazole C-4, $^2J_{C4,H3}$ = 8.5 Hz), 71.3 (OCH_2Si, ^1J = 136.3 Hz, $^3J_{OCH2Si,SiCH3}$ = 2.3 Hz), 60.0 (ester OCH_2, ^1J = 147.2 Hz, $^2J_{OCH2,CH3}$ = 4.5 Hz), 14.4 (ester CH_3, ^1J = 126.9 Hz, $^2J_{CH3,OCH2}$ = 2.5 Hz), -3.4 ($SiMe_3$, ^1J = 119.6 Hz); ir (dichloromethane): cm^{-1} 1707 (C=O); ms: m/z (%) 318 (M^+, 25), 317 (25), 304 (18), 303 (83), 276 (18), 275 (96), 273 (23), 262 (21), 261 (100), 200 (27), 199 (99), 187 (11), 186 (33), 185 (10), 172 (12), 144 (11), 118 (14), 91 (46), 89 (18), 77 (49), 75 (46), 73 (32), 61 (11), 59 (44), 51 (13).

Anal. Calcd. for $C_{16}H_{22}N_2O_3Si$: C, 60.35; H, 6.96; N, 8.80. Found: C, 60.68; H, 6.83; N, 8.92.

Ethyl 5-Methoxy-1-phenyl-1*H*-pyrazole-4-carboxylate (**8**).

To a stirred solution of **4a** (232 mg, 1 mmole) in 4 ml of dichloromethane were added 220 mg (1 mmole) of 40% aqueous tetrafluoroboric acid at 0°. Then 0.5 ml (1 mmole) of trimethylsilyldiazomethane (2*M* solution in *n*-hexane) were added dropwise and stirring was continued at 0°. Further three 0.17 ml portions of trimethylsilyldiazomethane (1 mmole in summary) were added in intervals of 30 minutes and stirring was continued for 30 minutes after the last addition. Then the reaction mixture was poured into water and extracted with dichloromethane. The combined organic phases were washed successively with saturated aqueous sodium bicarbonte solution and water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was recrystallized from diisopropylether to afford 148 mg (60%) of colorless crystals, mp 66-68° (lit [27] mp 67°); ^{1}H-nmr (deuteriochloroform): δ 7.92 (s, 1H, pyrazole H-3), 7.63 (m, 2H, Ph H-2,6), 7.44 (m, 2H, Ph H-3,5), 7.34 (m, 1H, Ph H-4), 4.31 (q, J = 7.1 Hz, 2H, OCH_2), 4.12 (s, 3H, 5-OCH_3), 1.36 (t, J = 7.1 Hz, ester CH_3); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 7.93 (s, 1H, pyrazole H-3), 7.61 (m, 2H, Ph H-2,6), 7.52 (m, 2H, Ph H-3,5), 7.41 (m, 1H, Ph H-4), 4.24 (q, J = 7.1 Hz, 2H, OCH_2), 4.09 (s, 3H, OCH_3), 1.28 (t, J = 7.1 Hz, ester CH_3); ^{13}C-nmr (deuteriochloroform): δ 162.1 (C=O, $^3J_{CO,OCH2}$ = 3.2 Hz), 155.6 (pyrazole C-5, $^3J_{C5,H3}$ = 4.5 Hz, $^3J_{C5,OCH3}$ = 4.3 Hz), 141.8 (pyrazole C-3, ^1J = 191.7 Hz), 137.7 (Ph C-1), 128.9 (Ph C-3,5), 127.5 (Ph C-4), 123.0 (Ph C-2,6), 100.5 (pyrazole C-4, $^2J_{C4,H3}$ = 8.7 Hz), 62.7 (OCH_3, ^1J = 147.7 Hz), 60.1 (OCH_2, ^1J = 147.4 Hz, $^2J_{OCH2,CH3}$ = 4.5 Hz), 14.3 (ester CH_3, ^1J = 127.0 Hz, $^2J_{CH3,OCH2}$ = 2.6 Hz); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 161.2 (C=O, $^3J_{CO,OCH2}$ = 3.3 Hz), 155.2 (pyrazole C-5, $^3J_{C5,H3}$ = 5.0 Hz, $^3J_{C5,OCH3}$ = 4.3 Hz), 141.3 (pyrazole C-3, ^1J = 191.8 Hz), 137.2 (Ph C-1), 129.1 (Ph C-3,5), 127.8 (Ph C-4), 123.1 (Ph C-2,6), 100.0 (pyrazole C-4, $^2J_{C4,H3}$ = 8.9 Hz), 62.9 (OCH_3, ^1J = 148.2 Hz), 59.7 (OCH_2, ^1J = 147.8 Hz, $^2J_{OCH2,CH3}$ = 4.5 Hz), 14.1 (ester CH_3, ^1J = 126.8 Hz, $^2J_{CH3,OCH2}$ = 2.6 Hz); ir: cm^{-1} 1705 (C=O); ms: m/z (%) 247 (M^++1, 14), 246 (M^+, 97), 245 (10), 202 (12), 201 (100), 200 (47), 199 (58), 186 (30), 173 (16), 172 (27), 157 (13), 144 (22), 118 (10), 91 (32), 77 (52), 53 (13), 51 (20).

Ethyl 2,3-Dihydro-1-methyl-3-oxo-2-phenyl-1*H*-pyrazole-4-carboxylate (**9**).

A mixture of **4a** (232 mg, 1 mmole), 1 ml of aqueous 1*N* sodium hydroxide, water (~ 2 ml) and dimethyl sulfate (252 mg, 2 mmoles) was vigorously stirred for 20 hours at room temperature. Then 2 ml of 1*N* sodium hydroxide solution were added and the suspension was stirred for a further 20 minutes. The mixture was then extracted with dichloromethane, the organic extract was washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was subjected to preparative tlc (eluent: dichloromethane-ethyl acetate, 9:1) to afford 39 mg (16%) of *O*-methyl derivative **8** (faster eluted component) and 80 mg (33%) of *N*-methyl compound **9** (slower eluted component) as colorless crystals of mp 143-145° (144-146° after recrystallization from diisopropyl ether-ethanol) (lit [28] mp 71-72°, lit [6] mp 71°, [29]). Pyrazolone **9** had ^{1}H-nmr (deuteriochloroform): δ 7.99 (s, 1H, pyrazole H-5), 7.49 (m, 2H, Ph H-3,5), 7.40 (m, 1H, Ph H-4), 7.31 (m, 2H, Ph H-2,6), 4.31 (q, J = 7.1 Hz, 2H, OCH_2), 3.38 (s, 3H, NCH_3), 1.35 (t, J = 7.1 Hz, 3H, ester CH_3); ^{13}C-nmr (deuteriochloroform): δ 162.5 (ester C=O, $^3J_{CO,OCH2}$ = 3.3 Hz, $^3J_{CO,H5}$ = 1.3 Hz), 161.7 (pyrazole C-3 (= pyrazolone C=O), $^3J_{C3,H5}$ = 7.0 Hz), 144.5 (pyrazole C-5, ^1J = 190.6 Hz, $^3J_{C5,NCH3}$ = 3.3 Hz), 133.0 (Ph C-1), 129.4 (Ph C-3,5), 128.6 (Ph C-4), 126.7 (Ph C-2,6), 99.9 (pyrazole C-4, $^2J_{C4,H5}$ = 4.3 Hz), 59.9 (OCH_2, ^1J = 147.3 Hz, $^2J_{OCH2,CH3}$ = 4.4 Hz), 37.2 (NCH_3, ^1J = 142.4 Hz, $^3J_{NCH3,H5}$ = 1.8 Hz), 14.3 (ester CH_3, ^1J = 126.9 Hz, $^2J_{CH3,OCH2}$ = 2.5 Hz); ir: cm^{-1} 1721 (ester C=O), 1638 (pyrazolone C=O); ms: m/z (%) 247 (M^++1, 12), 246 (M^+, 64), 202 (42), 201 (40), 175 (16), 174 (100), 173 (19), 145 (12), 121 (12), 104 (10), 91 (10), 83 (21), 82 (13), 77 (34), 53 (13), 51 (12).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.48; H, 5.57; N, 11.32.

Ethyl 1-Phenyl-1*H*-pyrazole-4-carboxylate (**10**) [15].

Compound **10** had ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 9.06 (s, 1H, pyrazole H-5), 8.11 (s, 1H, pyrazole H-3), 7.91 (m, 2H, Ph H-2,6), 7.50 (m, 2H, Ph H-3,5), 7.35 (m, 1H, Ph H-4), 4.25 (q, J = 7.0 Hz, 2H, OCH_2), 1.28 (t, J = 7.0 Hz, CH_3); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 162.0 (C=O, $^3J_{CO,OCH2}$ = 3.4 Hz), 141.6 (pyrazole C-3, ^1J = 190.7 Hz, $^3J_{C3,H5}$ = 7.1 Hz), 138.9 (Ph C-1), 131.0 (pyrazole C-5, ^1J = 194.2 Hz, $^3J_{C5,H3}$ = 3.3 Hz), 129.5 (Ph C-3,5), 127.2 (Ph C-4), 119.0 (Ph C-2,6), 116.2 (pyrazole C-4, $^2J_{C4,H3}$ = 8.9 Hz, $^2J_{C4,H5}$ = 6.9 Hz), 59.9 (OCH_2, ^1J = 147.9 Hz, $^2J_{OCH2,CH3}$ = 4.5 Hz) 14.2 (CH_3, ^1J = 126.8 Hz, $^2J_{CH3,OCH2}$ = 2.6 Hz); for ^{13}C-nmr (deuteriochloroform) see ref [15].

Ethyl 1-(2-Pyridinyl)-1*H*-pyrazole-4-carboxylate (**11**) [15].

Compound **11** had ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 8.93 (s, 1H, pyrazole H-5, 8.49 (m, 1H, pyridine H-6), 8.17 (s,

1H, pyrazole H-3), 8.02 (m, 1H, pyridine H-4), 7.94 (m, 1H, pyridine H-3), 7.42 (m, 1H, pyridine H-5), 4.25 (q, J = 7.1 Hz, 2H, OCH_2), 1.28 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C-nmr (deuteriodimethyl sulfoxide): δ 161.8 (C=O, $^3J_{CO,OCH2}$ = 3.3 Hz), 149.9 (pyridine C-2), 148.5 (pyridine C-6, ^1J = 181.8 Hz), 142.5 (pyrazole C-3, ^1J = 191.8 Hz, $^3J_{C3,H5}$ = 7.4 Hz), 139.8 (pyridine C-4, ^1J = 166.3 Hz), 129.5 (pyrazole C-5, ^1J = 195.9 Hz, $^3J_{C5,H3}$ = 3.5 Hz), 123.1 (pyridine C-5, ^1J = 166.9 Hz), 116.3 (pyrazole C-4, $^2J_{C4,H3}$ = 9.0 Hz, $^2J_{C4,H5}$ = 7.2 Hz), 112.5 (pyridine C-3, ^1J = 171.0 Hz), 60.1 (OCH_2, ^1J = 147.9 Hz, $^2J_{OCH2,CH3}$ = 4.5 Hz), 14.1 (CH_3, ^1J = 126.9 Hz, $^2J_{CH3,OCH2}$ = 2.6 Hz); for ^{13}C-nmr (deuteriochloroform) see ref [15].

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[29] Possibly, the product with mp 71-72° obtained upon reaction of the silver salt of **4a** with methyl iodide in lit [28] was not the assumed *N*-methylpyrazolone **9** but the corresponding *O*-methyl product **8** which has a very similar mp (66-68°).