Bicyclic [*b*]-Heteroannulated Pyridazine Derivatives. 9 [1]. Cyclization Reactions of 4,4-Dimethyl- and 4-Phenyltetrahydropyridazine-3,6-dione 3-Hydrazones with Esters of Keto Dicarboxylic Acids

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Bis(ethoxycarbonyl)alkylidene derivatives **4** and **5** of the respective title hydrazones were obtained in the reactions with diethyl oxomalonate, diethyl oxosuccinate, diethyl 2-oxoglutarate, and diethyl oxalopropionate as mixtures of geometric isomers with high predominance of one of them. On heating at 160-200° without any solvent or on refluxing in ethanol **4** cyclized to yield the corresponding pyridazino[6,1-*c*]triazines **6**, whereas heating of **5** gave, depending on the chain length, the corresponding pyrazolylpyridazines **8b** and **8d** or the pyridazinylpyridazine **8c**. X-ray analysis was used to determine the structures of **6** and **8**; the unit cell of **6c** was found to accommodate 16 molecules representing four conformational varieties. The different behavior of **4** and **5** in the cyclization reactions was interpreted in terms of the tautomeric equilibrium which was shifted towards the enamine form in **4**, and towards the imine form, in **5**. Transmission of a long-range chirality effect in **4d** and **5a-d** manifested itself in the ^{1}H nmr spectra as the magnetic non-equivalence of the CH_2 protons in one or both ester ethyl groups.

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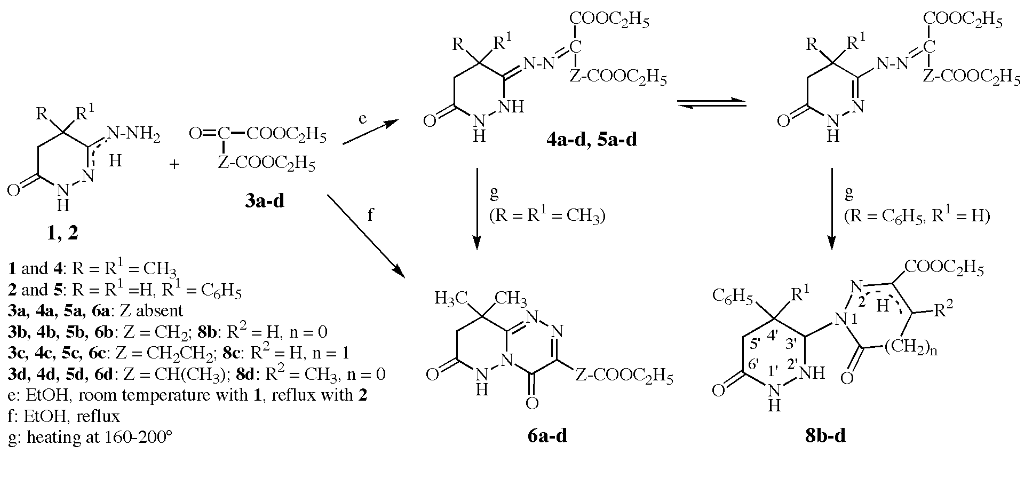
The 4-substituted tetrahydropyridazine-3,6-dione 3-hydrazones, readily available in the reaction of the appropriately 3-substituted 3-cyanopropionic esters with hydrazine hydrate [2], have been found earlier to be interesting and versatile starting materials in the preparation of bicyclic structures. Thus, the triazolo[4,3-*c*]pyridazine core was formed in the reaction with trifluoroacetic acid [3], whereas pyridazino[6,1-*c*]triazine derivatives were obtained in that with α-keto esters [4]. In either case, the intermediate linear acylation or condensation products underwent a spontaneous or enforced intramolecular cyclocondensation *via* the N2 pyridazine atom. With the most simple β-keto ester, ethyl acetoacetate, and some 4-aryltetrahydropyridazine-3,6-dione 3-hydrazones the cyclocondesation reaction run a different course to yield the derivatives of pyrazolylpyridazine formed by attack on the exocyclic (hydrazine) nitrogen atom [4].

Considering the distinction in the behavior of α- and β-keto esters we report now on the reactions of two tetrahydropyridazine-3,6-dione 3-hydrazones, namely their 4,4-dimethyl- (**1**) and 4-phenyl-substituted (**2**) derivatives, with esters of dicarboxylic keto acids in which the keto function is α relative to one, and α, β, or γ, to the other ester group. The main aim of the research was to find out which cyclocondensation pattem would predominate in the case when two ester groups were available. It was also expected that the easily convertible alkoxycarbonyl function in the bicyclic reaction products might tum out to be useful in the synthesis of compounds with potential biological activity.

Both **1** and **2** reacted in an ethanol solution with diethyl oxomalonate (**3a**), diethyl oxosuccinate (**3b**), diethyl 2-oxoglutarate (**3c**), and diethyl oxalopropionate (**3d**) to

Scheme 1



1 and **4**: R = R^1 = CH_3
2 and **5**: R = R^1 =H, R^1 = C_6H_5
3a, 4a, 5a, 6a: Z absent
3b, 4b, 5b, 6b: Z = CH_2; **8b**: R^2 = H, n = 0
3c, 4c, 5c, 6c: Z = CH_2CH_2; **8c**: R^2 = H, n = 1
3d, 4d, 5d, 6d: Z = $CH(CH_3)$; **8d**: R^2 = CH_3, n = 0
e: EtOH, room temperature with **1**, reflux with **2**
f: EtOH, reflux
g: heating at 160-200°

yield the respective condensation products **4a-d** and **5a-d.** The reaction with **1** occurred readily at room temperature whereas prolonged refluxing was required to effect the condensation with **2**. On the other hand, when **1** and the esters were made to react in refluxing ethanol, products of the subsequent intramolecular cyclocondensation (**6**) were in most cases highly predominant (Scheme 1).

In the ^{1}H- and ^{13}C nmr spectra of **4** and **5** some signals were split thus indicating the presence of two isomeric species, presumably the geometric isomers on the C=N bond formed in the condensation reaction. An analogous doubling of the ^{1}H nmr signals was observed in the spectrum of 4,4-dimethyltetrahydropyridazine-3,6-dione 3-(2-butylidene)hydrazone (**7**) prepared as a reference compound from **1** and 2-butanone [5]. It was assumed that a possible restriction of rotation about the N-N bond, which might lead to the formation of *s-cis/s-trans* isomers, could hardly be responsible for the phenomenon observed. No attempts were made to resolve the mixtures or to determine the configuration of the predominant isomer. Moreover, a magnetic non-equivalence of the CH_2 protons in one of the ester ethyl groups was noted in the ^{1}H nmr spectra of **4d** and **5a-c**. In the case of **5d**, the non-equivalence was observed in both ester groups. This phenomenon seems to be analogous to that observed earlier in the products of the condensation of **2** and its analogs with ethyl acetoacetate [4]. In the present case, however, close overlapping of the signals of both ester groups did not allow to make any detailed assignments. A particularly interesting case is that of **5d** where the fairly well resolved though rather complex ^{1}H nmr spectrum (Figure 1) indicates the presence of a roughly 1:1 mixture of isomers, presumably diastereoisomers. In the spectrum there are, therefore, signals of four distinct ester groups with magnetically nonequivalent CH_2 protons. Since a chiral carbon atom (in **5d** even two such atoms) is present in **4d** and **5a-d**, a long-range transmission of the chirality effects may be considered as the primary reason for the magnetic differentiation of the geminal protons.

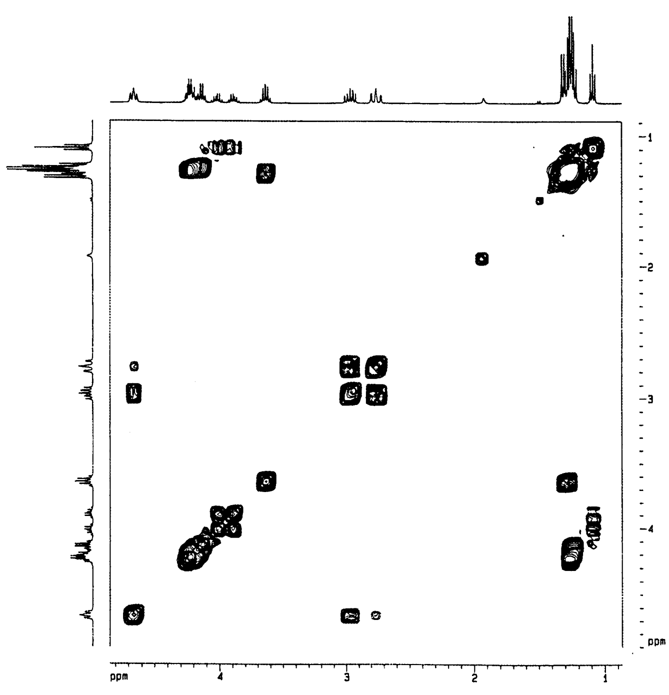


Figure 1. The ^{1}H nmr COSY spectrum of diethyl 2-[(1,4,5,6-tetrahydro-6-oxo-4-phenyl-3-pyridazinyl)hydrazono]-3-methylbutanedioate (**5d**).

The intramolecular cyclizations of **4** and **5**, which yielded **6** and **8**, respectively, were effected by heating these compounds at 160-200° without any solvent. Compounds **6** were also obtained by directly condensing **1** with the appropriate ester **3** in refluxing ethanol. In general, **4** cyclized more readily than **5**; irrespective of the reaction conditions **5a** failed to cyclize at all. The condensation of **2** with **3d** carried out in refluxing ethanol yielded both **5d** and **8d**, which were separated from one another by column chromatography.

Considering the possible tautomerism of **4** and **5** (cf. Scheme 1), the cyclizations could have occurred either *via* N2 with the formation of a pyridazinotriazine or *via* the hydrazine nitrogen atom with the formation of a ring not fused with the pyridazine. Earlier reports on similar cyclocondensations with various nitrogen heterocycles concemed mostly the acetoacetic esters which yielded compounds identified as the pyrazolyl-substituted heterocycles [6-9]. These assignments have been later substantiated by X-ray analysis of the cyclocondensation product obtained from the *p*-methyl-substituted derivative of **2** and ethyl acetoacetate [4].

In the case of **4a**, in which both ester groups are equivalent, the structure of the cyclization product could be determined as **6a** in advance; the formation of a 4-membered ring by attack on the hydrazine nitrogen atom was considered to be rather unlikely. However, as stated above, **5a** failed to give any cyclization product; only tarry products were obtained on heating this compound at 180-200° without any solvent or on refluxing in *N*-methyl-2-pyrrolidone. The original working hypothesis which assumed an unconditional cyclization preference of the α-ester group has been strongly shaken by this evidence. On the other hand, the informations derived from the ir and nmr spectra of the products obtained by cyclization of all other **4** and **5** did not allow to make any unequivocal structural assignments. It was, therefore, necessary to resort to the crystallographic analysis which made it possible to positively identify three compounds. Thus, the products obtained from **4c** and **4d** have been revealed as the pyridazinotriazine derivatives **6c** and **6d**, respectively, whereas that resulting from the cyclization of **5d** has been identified as the pyrazolylpyridazine **8d**. Their respective ORTEP drawings are shown in Figures 2-4, whereas all X-ray analysis details, selected geometrical data, and hydrogen bond geometry are collected in Tables 1-3, respectively [10].

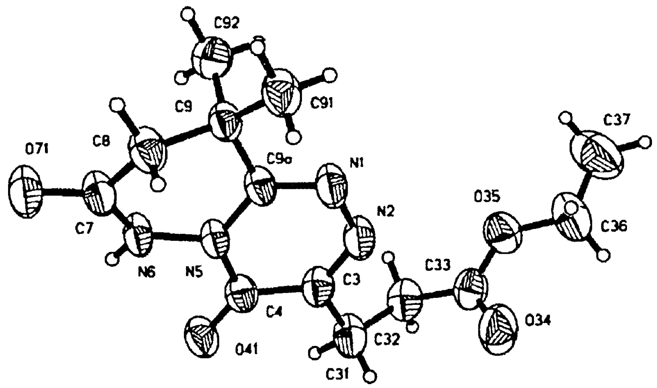
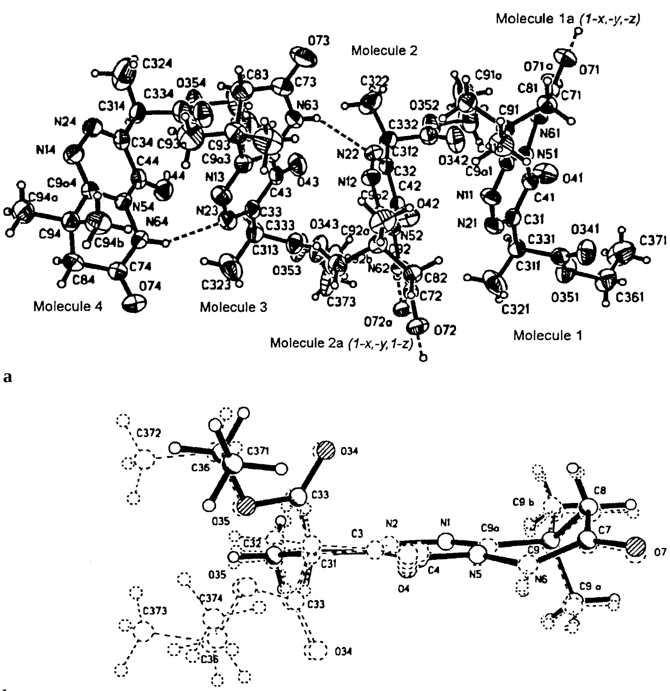


Figure 2. The ORTEP drawing of ethyl 6,7,8,9-tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino-[6,1-*c*]triazine]-3-propionate (**6c**).



a

b

Figure 3 (a) The ORTEP drawing of four conformationally different molecules in the crystal structure of ethyl 6,7,8,9-tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino-[6,1-*c*]triazine]-3-(2-propionate) (**6d**) with hydrogen bonds shown as dotted lines; (b) superposition of four molecules of **6d** with alignment of the Nitrogen atoms.

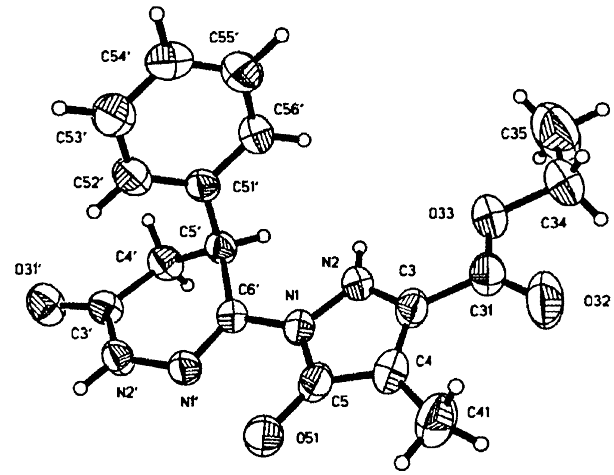


Figure 4. The ORTEP drawing of ethyl 1-(1,4,5,6-tetrahydro-6-oxo-4-phenylpyridazin-3-yl)-4,5-dihydro-4-methyl-5-oxo-1*H*-pyrazole-3-carboxylate (**8d**).

Figures 2 and 4 depict the respective structures of **6c** and **8d** clearly and completely. With **6d** the picture is by far more complex since as many as four molecules (denoted as 1, 2, 3, and 4, respectively) are to be found in an independent part of the monoclinic unit cell. They form two pairs of enantiomers; [1(*S*)-2(*R*) and 3(*S*)-4(*R*)]. In all four molecules, like in those of **6c** and **8d**, the half-chair conformation of the pyridazinotriazine core is essentially the same. However, irrespective of the enantiomeric form, the four molecules of **6d** differ from one another in the conformation of the ester fragment as it may be seen in Figure 3a.

Intermolecular hydrogen bonds N-H···O have been found in the crystal structures of all three investigated compounds (Table 3). In the triclinic cell of **6c** they link two molecules to form a dimer, while the molecules of **8d** are hydrogen-bonded to form a chain structure with altemately positioned phenyl substituents. In the crystals of **6d** the molecules 1 exist as a hydrogen-bonded (N6-H···O7) dimer (Figure 3 and Table 3); an analogous dimer is formed by molecules 2. The molecules of the other enantiomeric pair (3 and 4) are joined together by a N64-H···N23 bond, and by an analogous N63-H···N22 bond with the dimer of the molecules 2. This three-element system forms the fundamental crystal net (Figure 3), the pockets of which accomodate a dimer built of the molecules 1. The latter dimer is not hydrogen-bonded with any other elements of the crystal structure.

Attempts to grow satisfactory monocrystals of the remaining **6** and **8** were unsuccessful. Consequently, the nmr spectra of **6c, 6d**, and **8d** and of their precursors (**4c, 4d**, and **5d**, respectively) had to be used as a reference material in determining the structures of other **6** and **8**.

A particularly important information was derived from the fact that **4d** followed a different cyclization pathway than that of **5d**. It is noteworthy that both compounds, rather identical as far as the bulky ester portion of the molecules is concerned, seem to differ from one another only in the character of the substituent at the C5 carbon atom (aliphatic *vs.* aromatic). However, the essential difference in their cyclization pattem may also indicate a difference in the position of the proton involved in the tautomeric equilibrium shown in Scheme 1. It may be assumed, therefore, that this equilibrium is shifted towards protonation of the

Table 1

X-ray Structure Analysis of **6c**, **6d**, and **8d**

A. Crystal Parameters	**6c**	**6d**	**8d**
formula	$C_{13}H_{18}N_4O_4$	$C_{13}H_{18}N_4O_4$	$C_{17}H_{18}N_4O_4$
molecular weight	294.31	294.31	342.35
crystallization medium	ethanol	ethanol	ethanol
colour	colorless	yellowish	light yellow
crystal size, mm	0.1 x 0.1 x 0.4	0.2 x 0.2 x 0.3	0.1 x 0.2 x 0.3
cell dimensions	a = 5.8770(10) Å	a = 17.921(4) Å	a = 9.668(2) Å
	b = 9.181(2) Å	b = 18.597(4) Å	b = 7.828(2) Å
	c = 13.313(3) Å	c = 19.972(4) Å	c = 22.506(5) Å
	α= 82.23(3)°		
	β = 88.00(3)°	β = 116.56(3)°	β = 90.27(3)°
	γ = 83.97(3)°		
space group	P-1	$P2_1/n$	$P2_1/n$
molecules/unit cell	2	16	4
density calcd.	1.381 Mg/m^3	1.313 Mg/m^3	1.335 Mg/m^3
linear absorption factor, mm^{-1}	0.873	0.099	0.097
B. Refinement Parameters			
number of reflections	2488	28838	15931
non-zero reflections [1>4σ(I)]	2173	5517	2983
R-index	0.063	0.081	0.063
GOF	1.072	1.221	1.128
secondary extinction factor	0.184(13)	0.00092(19)	0.006(2)

Table 2

Selected Geometrical Data of **6c**, **6d**, and **8d**: Bond Lengths (Å) and Torsional Aangles (deg)

6c

N1-C9a	1.292(4)
N1-N2	1.378(3)
N2-C3	1.288(4)
N5-N6-C7-C8	-0.2(4)
N6-C7-C8-C9	34.9(4)
C7-C8-C9-C9a	-47.1(4)
C8-C9-C9a-N5	28.1(3)
N6-N5-C9a-C9	4.6(4)
C9a-N5-N6-C7	-21.1(4)

8d

N1'-C6'	1.278(3)
N1'-N2'	1.388(2)
C6'-N1	1.393(2)
N1-N2	1.362(2)
N1'-N2'-C3'-C4'	1.6(3)
N2'-C3'-C4'-C5'	-30.2(3)
C3'-C4'-C5'-C6'	39.9(2)
C4'-C5'-C6'-N1'	-27.2(3)
N2'-N1'-C6'-C5'	0.7(3)
C6'-N1'-N2'-C3'	14.6(3)

6d - Molecule 1

N11-C9a1	1.292(4)	N51-N61-C71-C81	-5.2(4)
N11-N21	1.386(4)	N61-C71-C81-C91	-39.1(3)
N21-C31	1.290(5)	C71-C81-C91-C9a1	58.0(3)
		C81-C91-C9a1-N51	-35.0(4)
		N61-N51-C9a1-C91	-7.6(4)
		C9a1-N51-N61-C71	31.3(4)

6d - Molecule 2

N12-C9a2	1.302(4)	N52-N62-C72-C82	2.9(5)
N12-N22	1.392(4)	N62-C72-C82-C92	38.8(4)
N22-C32	1.293(4)	C72-C82-C92-C9a2	-55.7(4)
		C82-C92-C9a2-N52	34.1(4)
		N62-N52-C9a2-C92	5.3(4)
		C9a2-N52-N62-C72	-27.3(5)

6d - Molecule 3

N13-C9a3	1.296(5)	N53-N63-C73-C83	-0.6(5)
N13-N23	1.385(4)	N63-C73-C83-C93	40.4(5)
N23-C33	1.294(5)	C73-C83-C93-C9a3	-55.7(5)
		C83-C93- C9a3-N53	34.5(4)
		N63-N53- C9a3-C93	4.0(4)
		C9a3-N53-N63-C73	-23.6(5)

6d - Molecule 4

N14-C9a4	1.302(4)	N54-N64-C74-C84	1.4(5)
N14-N24	1.392(4)	N64-C74-C84-C94	-42.5(5)
N24-C34	1.279(4)	C74-C84-C94-C9a4	58.7(4)
		C84-C94-C9a4-N54	-37.1(4)
		N64-N54-C9a4-C94	-1.8(5)
		C9a4-N54-N64-C74	22.8(5)

Table 3

Geometry of Hydrogen Bonds in **6c**, **6d**, and **8d** (in Å)

X-H···Y(symm. code)	X-H (Å)	H···Y (Å)	X-H···Y (Å)	X-H···Y (Å)	
		6c			
N6 - H6 ···O71(*-1-x, 1-y, 1-z*)	0.90	2.03	2.891	158.6	dimer
		6d			
N61-H61···O71 (*1-x,-y,-z*)	0.90	2.98	2.111	161.8	dimer
N62-H62···O72(*1-x,-y,1-z*)	0.89	2.15	3.021	162.9	dimer
N63-H63···N22	0.90	2.33	3.079	140.3	
N64-H64···N23(1+x,y,z)	0.90	2.21	2.971	142.2	
		8d			
N2'-H2'···O31'(*-1/2-x, 1/2 +y, 1/2-z*)	0.90	1.89	2.735	155.2	

endocyclic nitrogen atom in **4**, and of the exocyclic nitrogen atom, in **5**. In all probability similar tautomeric equilibria may distinguish **1** from **2**. Hence, the structure of the pyridazinotriazines **6** has been assigned to all products obtained by cyclization of **4**, while that of the pyrazolylpyridazines **8b** and **8d** and the pyridazinylpyridazine **8c**, to those resulting from the corresponding **5**. These structural assignments were consistent with the data obtained by nmr spectroscopy.

The identification of **8c** as ethyl 1-(1,4,5,6-tetrahydro-6-oxo-4-phenylpyridazin-3-yl)-1,4,5,6-tetrahydro-6-oxopyridazine-3-carboxylate (**8c**) has been supported by comparing its ^{1}H nmr spectrum with that of its precursor (**5c**). In the latter, both CH_2 groups of the freely rotating ethoxycarbonylethyl substituent manifested themselves as nearly regular triplets, whereas very complex multiplets observed in that of **8c** were considered to indicate incorporation of these groups into a rigid cyclic structure.

EXPERIMENTAL

Melting points were determined in a Büchi apparatus and are reported uncorrected. The ir spectra were recorded in potassium bromide pellets on a Perkin-Elmer 298 spectrophotometer. ^{1}H- and ^{13}C nmr spectra were taken with Varian 300 MHz and Bruker 400 MHz instruments with TMS as intemal standard. Mass spectra were run by the electron impact technique at 70 eV on an AND-604 instrument. Microanalyses were carried out on a Perkin-Elmer C-H-N analyzer. Merck DC-Alufolien with Kieselgel 60 F_{254} were used in tlc purity checking; the developing system consisted of a chloroform-ethanol 9:1 mixture. All yield data refer to recrystallized, chromatographically homogeneous compounds with consistent elemental analysis data.

General Procedures for the Condensation of 4,4-Dimethyl- (**1**) and 4-Phenyltetrahydropyridazine-3,6-dione 3-Hydrazone (**2**) with Carbonyl Compounds.

Method A.

A mixture of the pyridazine derivative **1** and the appropriate carbonyl compound was stirred in ethanol at room temperature. When it became homogeneous (2-5 days), stirring was continued for 48 hours to complete the reaction. The slightly yellow or greenish solution was evaporated under reduced pressure and the solid or resinous residue was recrystallized from an appropriate solvent. Detailed data are given separately for the individual compounds.

Method B.

A mixture of the pyridazine derivative (**1** or **2**) and the appropriate carbonyl compound was refluxed with ethanol for several hours. The crude product left upon evaporation of the excess ethanol was purified by recrystallization from an appropriate solvent; column-chromatographic purification was required in some cases. The reactions starting with **1** and carried out at an elevated temperature yielded in most cases, either as the only product or at least as a by-product, the corresponding bicyclic compound **6** formed by subsequent cyclization of the intermediate **4**. Detailed data are given separately for individual compounds.

Diethyl [(1,4,5,6-Tetrahydro-4,4-dimethyl-6-oxo-3-pyridazinyl)hydrazono]propanedioate (**4a**).

This compound was obtained according to Method B by refluxing for 35 hours **1** (0.5 g, 0.0032 mole) and diethyl oxomalonate (**3a**, 0.7 g, 0.0040 mole) in 30 mL of ethanol. Repeated recrystallization from ethanol (2 x 2.5 mL) yielded 0.58 g (58%) of **4a**, mp 131-134°; ir: ν 3200 (NH), 1744, 1688, and 1668 (C=O) cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 1.31 (t, J = 7.1 Hz, 3H, ester CH_3), 1.34 (t, J = 7.1 Hz, 3H, ester CH_3), 1.31 (s, 2 x 3H, CCH_3), 2.41 (s, 2H, endocyclic CH_2), 4.29 (q, J = 7.1, 2H, ester CH_2), 4.32 ppm (q, J = 7.1 Hz, 2H, ester CH_2).

Anal. Calcd. for $C_{13}H_{20}N_4O_5$ (312.32): C, 49.99; H, 6.45; N, 17.94. Found: C, 49.80; H, 6.49; N, 18.10.

Diethyl 2-[(1,4,5,6-Tetrahydro-4,4-dimethyl-6-oxo-3-pyridazinyl)hydrazono]butanedioate (**4b**).

This compound was obtained according to Method A by stirring for 5 days the mixture of 0.3 g (0.0019 mole) of **1** and 0.42 g (0.0022 mole) of diethyl oxosuccinate (**3b**) in 17 mL of ethanol. The crude product was repeatedly washed with cold ethanol (2 x 2.5 mL) to yield 0.11 g (17%) of **4b**, mp 156-159°; ν 3300 (NH), 1732, 1694, 1664 (C=O) cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 1.21 (t, J = 7.1 Hz, 3H, ester CH_3), 1.29 (t, J = 7.1 Hz, 3H, ester CH_3), 1.29 (s, 6H, 2 x CCH_3), 2.39 (s, 2H, endocyclic CH_2), 3.62 (s, 2H, CH_2COO), 4.12 (q, J = 7.1 Hz, 2H, ester CH_2), 4.26 (q, J = 7.1 Hz, 2H, ester CH_2), 12.25 ppm (s, lH, NH).

Anal. Calcd. for $C_{14}H_{22}N_4O_5$ (326.35): C, 51.53; H, 6.79; N, 17.17. Found: C, 51.32; H, 6.80; N, 17.34.

Diethyl 2-[(1,4,5,6-Tetrahydro-4,4-dimethyl-6-oxo-3-pyridazinyl)hydrazono]pentanedioate (**4c**).

This compound was obtained according to Method A by stirring for 7 days the mixture of 0.2 g (0.00128 mole) of **1** and 0.29 g (0.00143 mole) of diethyl 2-oxoglutarate (**3c**) in 15 mL of ethanol. Repeated low-temperature recrystallization from ethanol (2 x 2.5 mL) yielded 0.28 g (65%) of **4c**, mp 107-110°; ir: ν 3300 (NH), 1720, 1696, 1656 (C=O) cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 1.21 (t, J = 7.1 Hz, 3H, ester CH_3), 1.31 (t, J = 7.1 Hz, 3H, ester CH_3), 1.32 (s, 2 x 3H, CCH_3), 2.37 (s, 2H, endocyclic CH_2), 2.66-2.81 (m, 4H, CH_2CH_2), 4.09 (q, J = 7.1 Hz, 2H, ester CH_2), 4.26 (q, J = 7.1 Hz, 2H, ester CH_2), 8.50 (diffuse s, 1H, NH), 9.70 ppm (diffuse s, 1H, NH).

Anal. Calcd. for $C_{15}H_{24}N_4O_5$ (340.37): C, 52.93; H, 7.11; N, 16.46. Found: C, 52.83; H, 7.24; N, 16.12.

Diethyl 2-[(1,4,5,6-tetrahydro-4,4-dimethyl-6-oxo-3-pyridazinyl)hydrazono]-3-methylbutanedioate (**4d**).

This compound was obtained according to Method A by stirring for 3 days the mixture of 0.47 g (0.003 mole) of **1** and 0.7 g (0.0035 mole) of diethyl 2-oxalopropionate (**3d**) in 8 mL of ethanol. Repeated washing of the crude product with ethanol (2 x 4.5 mL) yielded 0.63 g (62%) of **4d**, mp 144-146°; ir: ν 3248 and 3204 (NH), 1732, 1692, 1664, and 1632 cm^{-1} (C=O and C=N); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.24 (t, J = 7.1 Hz, 3H, ester CH_3), 1.32 (t, J = 7.3 Hz, 3H, ester CH_3), 1.33 (s, 6H, 2 x CCH_3), 1.48 (d, J = 7.25 Hz, 3H, $CHCH_3$), 2.42 (s, 2H, endocyclic CH_2), 3.76 (q, J = 7.25 Hz, 1H, $CHCH_3$)) 4.15 (q, J = 7.1 Hz, 2H, ester CH_2), 4.23-4.35 (m, 2H, non-equivalent ester CH_2), 8.41 (s, 1H, NH), 12.20 ppm (s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 13.9 (ester CH_3), 14.2 (ester CH_3), 14.9 ($CHCH_3$), 24.0 (2 x CCH_3), 33.6 (CCH_3), 41.8 (endocyclic CH_2), 44.7 ($CHCH_3$), 61.0 (ester CH_2), 61.7 (ester CH_2 with nonequivalent H), 135.0 (C=N), 151.5 (C=N), 162.7 (ester C=O), 166.6 (endocyclic C=O), 172.8 ppm (ester C=O).

Anal. Calcd. for $C_{15}H_{24}N_4O_5$ (340.37): C, 52.93; H, 7.11; N, 16.46. Found: C, 52.77; H, 7.07; N, 16.41.

Diethyl [(1,4,5,6-Tetrahydro-6-oxo-4-phenyl-3-pyridazinyl)-hydrazono]propanedioate (**5a**).

This compound was obtained according to Method B by refluxing for 48 hours 0.65 g (0.0032 mole) of **2** and 0.70 g (0.0046 mole) of **3a** in 60 mL of ethanol. Repeated recrystallization from ethanol (2 x 4.5 mL) yielded 0.89 g (78%) of **5a**, mp 146-149°; ir: ν 3328 (NH), 1688 (C=O) cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 1.32 (t, J = 7.1 Hz, 3H, ester CH_3), 1.34 (t, J = 7.1, 3H, ester CH_3), 2.79 (dd, ^{3}J = 1.8 Hz, ^{2}J = 17.2 Hz, 1H, endocyclic C*H*H), 3.01 (dd, $^{3'}$J = 8.4 Hz, ^{2}J = 17.2 Hz, 1H, endocyclic CH*H*), 4.29 (q, J = 7.1 Hz, 2H, ester CH_2), 4.22-4.35 (m, 2H, unequivalent ester CH_2), 4.74 (dd, ^{3}J = 1.8 Hz, $^{3'}$J = 8.4 Hz, 1H, CH), 7.26-7.29 (m, 5H, aromatic CH), 8.8 (diffuse s, 1H, NH), 12.38 ppm (diffuse s, 1H, NH).

Anal. Calcd. for $C_{17}H_{20}N_4O_5$ (360.36): C, 56.66; H, 5.59; N, 15.55. Found: C, 56.41, 5.57; N, 15.52.

Diethyl 2-[(1,4,5,6-Tetrahydro-6-oxo-4-phenyl-3-pyridazinyl)-hydrazono]butanedioate (**5b**).

This compound was obtained accoding to Method B by refluxing for 26 hours the mixture of 0.65 g (0.0032 mole) of **2** and 0.70 g (0.0037 mole) of **3b** in 60 mL of ethanol. Repeated recrystallization from ethanol (2 x 6.5mL) yielded 0.66 g (56%) of **5b**, mp 160-163°; ir: ν 3236 (NH), 1740, 1704, 1668 cm^{-1} (C=O); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.08 (t, J = 7.1 Hz, 3H, ester CH_3), 1.33 (t, J = 7.1 Hz, 3H, ester CH_3), 2.68 (d, J = 17.1 Hz, 1H, endocyclic C*H*H), 2.97 (dd , ^{3}J = 7.5 Hz, ^{2}J = 17.1 Hz, 1H, endocyclic CH*H*), 3.77 (s, 2H, CH_2COO), 3.95 (q, J = 7.1 Hz, 2H, ester CH_2), 4.15-4.33 (m, 2H, non-equivalent ester CH_2), 4.97 (d, J = 7.5 Hz, 1H, CH), 7.25-7.37 (m, 5H, aromatic CH), 10.66 (s, 1H, NH), 11.38 ppm (s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 14.0 and 14.25 (CH_3), 32.1 and 33.7 (CH_2), 36.1 (CH), 61.1 and 61.4 (ester CH_2), 127.5, 127.8, 129.0, 132.0, and 138.0 (aromatic C), 155.1 (C=N), 164.5, 167.8, and 168.3 ppm (C=O).

Anal. Calcd. for $C_{18}H_{22}N_4O_5$ (374.39): C, 57.75; H, 5.92; N, 14.96. Found: C, 57.72; H, 6.00; N, 14.78.

Diethyl 2-[(1,4,5,6-Tetrahydro-6-oxo-4-phenyl-3-pyridazinyl)-hydrazono]pentanedioate (**5c**).

This compound was obtained according to Method B by refluxing for 26 hours 0.65 g (0.0032 mole) of **2** and 0.8 g (0.0039 mole) of **3c** in 65 mL of ethanol. Repeated recrystallization from ethanol (2 x 6 mL) yielded 0.87 g (70%) of **5c**, mp 162-165°; ir: ν 3200 (NH), 1706, 1672 (C=O), 1648 cm^{-1} (C=O or C=N); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.16 (t, J = 7.1 Hz, 3H, ester CH_3), 1.35 (t, J = 7.1 Hz, 3H, ester CH_3), 2.53 (t, J = 6.9 Hz, 2H, $N{=}CCH_2$), 2.71 (d, ^{2}J = 17 Hz, 1H, endocyclic C*H*H), 2.83 (t, J = 6.9 Hz, 2H, CH_2COO), 2.98 (dd , ^{2}J = 17.1 Hz, ^{3}J = 8.4 Hz, 1H, endocyclic CH*H*), 4.04 (q, J = 7.1 Hz, 2H, ester CH_2), 4.18-4.33 (m, 2H, non-equivalent ester CH_2), 4.82 (d, ^{3}J = 8.1 Hz, 1H, endocyclic CH), 7.24-7.38 (m, 5H, aromatic H), 9.53 (s, 1H, NH), 10.61 ppm (s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 14.1 (CH_3), 14.3 (CH_3), 20.8 (endocyclic CH_2), 30.8 ($N{=}CCH_2$), 33.9 (CH_2COO), 36.5 (endocyclic CH), 61.0 (ester CH_2), 61.3 (ester CH_2), 127.5, 127.7, and 129.0 (aromatic CH), 138.0 and 138.2 (exocyclic C=N and aromatic quatemary C), 153.6 (endocyclic C=N), 164.5 (ester C=O), 167.5 (endocyclic C=O), 173.5 ppm (ester C=O).

Anal. Calcd. for $C_{19}H_{24}N_4O_5$ (388.42): C, 58.75; H, 6.23; N, 14.42. Found: C, 59.00; H, 6.14; N, 14.53.

Diethyl 2-[(1,4,5,6-Tetrahydro-6-oxo-4-phenyl-3-pyridazinyl)-hydrazono]-3-methylbutanedioate (**5d**) (an approx. 1:1 mixture of diastereroisomers) and Ethyl 1-(1,4,5,6-Tetrahydro-6-oxo-4-phenylpyridazin-3-yl)-4,5-dihydro-4-methyl-5-oxo-1*H*-pyrazole-3-carboxylate (**8d**).

These compounds were obtained according to Method B by refluxing for 28 hours 1.13 g (0.0055 mole) of **2** and 1.34 g (0.0066 mole) of **3d** in 80 mL of ethanol. Chromatography of the oily crude product with chloroform on a column packed with silicagel 60 (70-230 mesh) yielded 0.8 g (60%) of **5d** as the head fraction. It solidified on prolonged standing and finally was purified by recrystallization from cyclohexane (100 mL) and identified as an 1:1 mixture of diastereoisomeric **5d**, mp 84-90°. The tail fractions of the chromatography (0.260 g), purified by recrystallization from benzene (2 x 2 ml) gave 0.183 g (9.7%) of **8d**, mp 182-186°. ^{1}H nmr of **5d** (400 MHz, deuteriochloroform): δ 1.09 (t, J = 7.1 Hz, 3H, ester CH_3), 1.21-1.32 (m, 15H, 3 x ester CH_3 and 2 x $CHCH_3$), 2.72-2.80 (m, 2H, 2 x endocyclic C*H*H), 2.93-3.02 (m, 2H, 2 x endocyclic CH*H*), 3.60-3.68 (m, 2H, 2 x $CHCH_3$), 3.87-4.29 (m, 8H, 4 x non-equivalent ester CH_2), 4.64-4.68 (m, 2H, 2 x endocyclic CH), 7.24-7.33 (m, 10H, 2 x aromatic CH), 8.55 and 8.58 (2 x s, 2H, 2 x NH), 12.08 and 12.10 ppm (2 x s, 1H, 2 x NH); ^{13}C nmr of **5d** (400 MHz, deuteriochloroform): δ 13.9, 13.95, 14.05, 14.2, 14.45, and 15.0 (4 x ester CH_3 and 2 x $CHCH_3$), 34.55 and 34.7 (2 x C5), 36.25 and 36.55 (2 x C4), 43.15 and 43.45 (2 x CH_3CH), 60.8, 60.95, 61.35, and 61.4 (4 x ester CH_2), 127.1, 127.15, 127.7, 127.75, 129.1, 129.15, 137.1, and 137.5 (2 x aromatic C), 130.1 and 130.8 (2 x N=*C*COOEt), 151.51 and 151.65 (2 x C3), 162.0 and 162.05 (2 x ester C=O), 166.1 and 166.25 (2 x C6), 172.9 and 173.55 ppm (2 x ester C=O). ^{1}H nmr of **8d** (400 MHz, deuteriochloroform): δ 1.38 (t, J = 7.1 Hz, 3H, ester CH_3), 2.09 (s, 3H, 4-CH_3), 2.91 (d, J = 17.4 Hz, 1H, 5'-C*H*H), 3.09 (dd, ^{3}J = 8.0 Hz, ^{2}J = 17.4 Hz, 5'-CH*H*), 4.33-4.41 (m, 2H, ester CH_2), 5.26 (broad d, J = 7.6 Hz, 1H, 4'-CH), 7.24-7.30 (m, 5H, aromatic CH), 9.64 (broad s, 1H, NH), 9.82 ppm (broad s, 1H, NH); ^{13}C nmr of **8d** (400 MHz, deuteriochloroform): δ 7.1 (4-CH_3), 14.25 (ester CH_3), 33.75 (C5'), 36.95 (C4'), 61.1 (ester CH_2), 100.6 (C4), 127.1, 128.3, 129.35, and 135.95 (aromatic

C), 143.35 (C5 or C3), 151.45 (C3'), 152.3 (C3 or C5), 162.55 (ester C=O), 166.7 ppm (C6').

Anal. of **5d**. Calcd. for $C_{19}H_{24}N_4O_5$ (388.42): C, 58.75; H, 6.23; N, 14.42. Found: C, 58.84; H, 6.17; N, 14.30.

Anal. of **8d**. Calcd. for $C_{17}H_{18}N_4O_4$ (342.35): C, 59.64; H, 5.30; N, 16.37. Found: C, 59.97; H, 5.31; N, 16.26.

4,4-Dimethyltetrahydropyridazine-3,6-dione 3-(2-Butylidene)-hydrazone (**7**).

This compound was obtained according to Method A by stirring for 16 hours the mixture of 0.47 g (0.003 mole) of **1**, 1.5 mL of 2-butanone, and 2 mL of methanol. The crude product (a yellowish gum) was treated with 2 mL of nitromethane and next the precipitated solid recrystallized from 1.5 mL of nitromethane to yield upon thorough cooling 0.45 g (71%) of **7**, mp 133-134.5. ^{1}H nmr (400 MHz, deuteriochloroform) of the major isomer: δ 1.13 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.30 (s, 6H, 2 x CCH_3), 1.90 (s, 3H, $=CCH_3$), 2.37 (s, 2H, endocyclic CH_2), 2.38 (q, J = 7.5 Hz, CH_2CH_3), 7.03 (broad s, 1H, NH), 8.54 ppm (broad s, 1H, NH); ^{1}H nmr (400 MHz, deuteriochloroform) of the minor isomer: δ 1.16 (t, J = 7.7 Hz, 3H, CH_2CH_3), 1.28 (s, 6H, 2 x CCH_3), 2.08 (s, 3H, $=CCH_3$), 2.35 (q, J = 7.6 Hz, CH_2CH_3), 2.37 (s, 2H, endocyclic CH_2), 7.03 (broad s, 1H, NH), 8.54 ppm (broad s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform) of the major isomer: δ 11.2 (CH_2CH_3), 14.2 ($=CCH_3$), 24.1 (2 x CCH_3), 32.25 (CH_2CH_3), 33.6 (C4), 42.0 (C5), 153.25 (C3 or $=CCH_3$), 156.8 ($=CCH_3$ or C3), 166.7 ppm (C6); ^{13}C nmr (400 MHz, deuteriochloroform) of the minor isomer: δ 9.5 (CH_2CH_3), 22.75 ($=CCH_3$), 23.0 (CH_2CH_3), 24.35 (2 x CCH_3), 32.25 (CH_2CH_3), 33.6 (C4), 42.0 (C5), 153.25 (C3 or $=CCH_3$), 156.8 ($=CCH_3$ or C3), 166.7 ppm (C6).

General Procedure for Cyclization of **4** and **5**.

Method C.

The appropriate **4** or **5** was heated without any solvent in an oil bath kept at 160-210° until evolution of the gaseous reaction products (ethanol) ceased. Upon cooling, the vitrous melt was recrystallized from a suitable solvent. Detailed preparative data are given for individual compounds below.

Altematively, Method B was used to obtain some bicyclic compounds **6** or **8** directly from **1** and **2**, respectively, and the appropriate keto ester.

Ethyl 6,7,8,9-Tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino-[6,1-*c*]triazine-3-carboxylate (**6a**).

This compound was obtained according to Method C by heating 0.5 g (0.0016 mole) of **4a** for 1 hour at 190-200°. Repeated recrystallization from ethanol (2 x 5 mL) yielded 0.33 g (78%) of **6a**, mp 153-156°. Ir: ν 1744, 1720, and 1686 cm^{-1} (C=O); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.40 (t, J = 7.15 Hz, 3H, ester CH_3), 1.55 (s, 3H, CCH_3), 1.57 (s, 3H, CCH_3), 2.74 (s, 2H, endocyclic CH_2), 4.43 ppm (q, J = 7.15 Hz, 2H, ester CH_2); ^{13}C nmr (400 MHz, deuteriochloroform): 14.0 (ester CH_3), 24.6 (2 x CCH_3), 36.3 (C9), 41.1 (C8), 62.8 (ester CH_2), 143.1 (C3 or C4), 147.6 (C4 or C3), 154.5 (C9a), 161.0 (ester C=O), 165.8 ppm (C7); ms: m/z 266 (M$^+$).

Anal. Calcd. for $C_{11}H_{14}N_4O_4$ (266.25): C, 49.62; H, 5.30; N, 21.04. Found: C, 49.41; H, 5.21; N, 21.09.

Ethyl 6,7,8,9-Tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino[6,1-*c*]triazine-3-acetate (**6b**).

This compound was obtained according to Method B by refluxing for 27 hours the mixture of 0.6 g (0.0038 mole) of **1** and 0.86 g (0.0046 mole) of **3b** in 50 mL of ethanol. Repeated recrystallization from ethanol (2 x 15 mL) yielded 0.41 g (39%) of **6b**, mp 205-208°. Ir: ν 3230, 1705, 1680, 1655 cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.28 (t, J = 7.1 Hz, 3H, ester CH_3), 1.54 (s, 6H, 2 x CH_3), 2.68 (s, 2H, pyridazine CH_2), 3.93 (s, 2H, exocyclic CH_2), 4.21 (q, J = 7.1 Hz, 2H, ester CH_2), 11.42 (s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform-deuteriotrifluoroacetic acid 2:3): δ 14.0 (ester CH_3), 23.7 (2 x CH_3), 37.9 (C9), 37.95 (exocyclic CH_2), 40.4 (C8), 65.95 (ester CH_2), 145.9, 154.6, 160.65, 169.55, and 171.5 ppm (C=N and C=O); ms: m/z 280 (M$^+$).

Anal. Calcd. for $C_{12}H_{16}N_4O_4$ (280.28): C, 51.42; H, 5.75; N, 19.99. Found: C, 51.47; H, 5.65; N, 19.81.

Ethyl 6,7,8,9-Tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino[6,1-*c*]triazine]-3-propionate (**6c**).

This compound was obtained according to Method B by refluxing for 26 hours the mixture of 0.5 g (0.0032 mole) of **1** and 0.75 g (0.0037 mole) of **3c** in 27 mL of ethanol. Repeated recrystallization from ethanol (2 x 2.5 mL) yielded 0.5 g (54%) of **6c**, mp 143-145°; ir: ν 1738, 1698, 1676 cm^{-1} (C=O); ^{1}H nmr (400 MHz, deuteriochloroform): δ 1.26 (t, J = 7.15 Hz, 3H, ester CH_3), 1.54 (s, 6H, 2 x CCH_3), 2.70 (s, 2H, endocyclic CH_2), 2.88 and 3.20 (2 x t, 2 x 2H, CH_2CH_2), 4.14 (q, 2H, ester CH_2), 10.5 ppm (diffuse s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 14.1 (ester CH_3), 24.7 (2 x CCH_3), 25.8 and 29.45 (CH_2CH_2), 36.6 (C9), 41.6 (C8), 60.6 (ester CH_2), 145.2 (C4 or C3), 151.3 (C9a), 157.6 (C3 or C4), 165.9 (C7), 172.3 ppm (ester C=O); ms: m/z 294 (M$^+$).

Anal. Calcd. for $C_{13}H_{15}N_4O_4$ (294.31): C, 53.11; H, 6.16; N, 19.03. Found: C, 52.99; H, 6.05; N, 19.13.

Ethyl 6,7,8,9-Tetrahydro-9,9-dimethyl-4,7-dioxo-4*H*-pyridazino[6,1-*c*]triazine]-3-(2-propanoate) (**6d**).

This compound was prepared according to Method C by heating for 2 hours 1.0 g (0.0029 mole) of **4d** at 190-200°. Repeated recrystallization from ethanol (2 x 4 mL) yielded 0.48 g (63%) of **6d**, mp 145-147°; ir: ν 3200, 3140 (NH), 1728, 1696 cm^{-1} (C=O); ^{1}H nmr (400 MHz, deuteriochlorofom): δ 1.26 (t, J = 7.1 Hz, 3H, ester CH_3), 1.55 and 1.57 (2 x s, 6H, 9-CH_3), 1.62 (d, J = 7.2 Hz, 3H, $CHCH_3$), 2.65-2.75 (m, 2H, 8-CH_2 with non-equivalent H), 4.14-4.23 (m, 3H, ester CH_2 and $CHCH_3$), ~10 ppm (diffuse s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 14.0 (ester CH_3), 14.1 ($CHCH_3$), 24.8 and 24.85 (2 x 9-CH_3), 35.9 (C9), 41.7 (C8), 42.15 ($CHCH_3$), 61.5 (ester CH_2), 144.75 (C4 or C3), 151.9 (C9a), 157.4 (C3 or C4), 165.55 (C7), 171.6 ppm (ester C=O); ms: m/z 294 (M$^+$).

Anal. Calcd. for $C_{13}H_{18}N_4O_4$ (294.31): C, 53.11; H, 6.16; N, 19.03. Found: C, 53.14; H, 6.12; N, 19.16.

Ethyl 1-(1,4,5,6-Tetrahydro-6-oxo-4-phenylpyridazin-3-yl)-4,5-dihydro-5-oxo-1*H*-pyrazole-3-carboxylate (**8b**).

This compound was obtained according to Method C by heating for 1 hour 0.25 g (0.00066 mole) of **5b** at 190-200°. The crude product was repeatedly extracted with hot ethanol to yield 0.13 g (60%) of **8b**, mp 243-246°; ir: ν 3220 (NH), 1708 and 1672 (C=O), 1648 (C=O or C=N); ^{1}H nmr (400 MHz, deuteriochloroform-deuteriotrifluoroacetic acid 2:3): δ 1.38 (t, J = 7.15 Hz, 3H, ester CH_3), 3.41 (dd , ^{2}J = 17.7 Hz, ^{3}J = 6.4 Hz, 1H, pyridazine CHH), 3.52 (dd , ^{2}J = 17.7 Hz , $^{3'}$J = 10.9 Hz, 1H, pyridazine CHH), 4.06 (d, J = 17.3 Hz, 1H, pyrazole CHH), 4.15 (d, J = 17.3 Hz, 1H, pyrazole CHH), 4.37 (q, J = 7.15 Hz, 2H, ester CH_2), 5.11

(dd, ^3J = 6.4 Hz, $^{3'}J$ = 10.9 Hz, 1H, pyridazine CH), 7.27-7.54 ppm (m, 5H, aromatic CH); ^{13}C nmr (400 MHz, deuteriochloroform-deuteriotrifluoroacetic acid 2:3): δ 13.95 (ester CH_3), 33.2 (C5'), 37.9 (C4), 41.65 (C4'), 65.65 (ester CH_2), 129.3, 129.55, 131.75, and 132.25 (aromatic C), 145.4, 154.25, 156.95, 169.8, and 171.35 ppm (C=O and C=N); ms: m/z 328 (M^+).

Anal. Calcd. for $C_{16}H_{16}N_4O_4$ (328.32): C, 58.53; H, 4.91; N, 17.06. Found: C, 58.34; 5.00; N, 17.09.

Ethyl 1-(1,4,5,6-Tetrahydro-6-oxo-4-phenylpyridazin-3-yl)-1,4,5,6-tetrahydro-6-oxopyridazine-3-carboxylate (**8c**)

This compound was obtained according to Method C by heating 0.2 g (0.00051 mole) of **5c** for 1 hour at 190-200°. Repeated recrystallization from ethanol (2 x 4 mL) yielded 0.13 g (77%) of **8c**, mp 162-165°. ir: ν 1722, 1684 (C=O); ^1H nmr (400 MHz, deuteriochloroform): δ 1.24 (t, J = 7.15 Hz, 2H, ester CH_3), 2.78-2.93 (m, 2H, CH_2CH_2), 3.08-3.27 (m, 4H, CH_2CH_2 and 5'-CH_2), 4.11 (q, 2H, ester CH_2), 4.69 (t, J = 5.5 Hz, 4'-CH), 7.30-7.40 (m, 5H, aromatic CH), 10.2 ppm (diffuse s, 1H, NH); ^{13}C nmr (400 MHz, deuteriochloroform): δ 14.2 (ester CH_3), 25.95 and 29.65 (CH_2CH_2), 33.2 (C5'), 40.75 (C4'), 60.7 (ester CH_2), 127.3, 128.6, 129.3, and 134.2 (aromatic C), 145.25 (C3 or C6), 147.8 (C3'), 157.9 (C6 or C3), 166.4 (C6'), 172.4 ppm (ester C=O); ms: m/z 342 (M^+).

Anal. Calcd. for $C_{17}H_{18}N_4O_4$ (342.35): C, 59.64; H, 5.30; N, 16.37. Found: C, 59.65; H, 5.28; N, 16.54.

Crystal X-ray Analysis of **6c**.

Preliminary data were obtained with a KM4 four-cycle diffractometer; the accurate cell dimensions were determined by the least-squares refinement from the angular settings of 25 reflections located within $10<\theta<40°$. A crystal of 0.1 x 0.1 x 0.4 mm was selected for the experiment. The diffraction data were collected on a KM4 diffractometer using graphite monochromated CuKα radiation at room temperature; ω/2θ scans were made for θ < 62° [h: -6/6, k: -10/10, l: -1/15]; no absorption correction was applied. The intensities of three standard reflections monitored every 100 reflections showed no significant fluctuation; 2488 reflections were measured, of which 2173 reflections were considered observed using the criterion $F_o > 4\sigma(F_o)$. The structure was solved by a direct method (SHELXTL-PC) [11].The E-map yielded positions for all non-hydrogen atoms. Full-matrix least-squares refinement was carried out on F's using anisotropic temperature factors for all nonhydrogen atoms; the starting positions of all hydrogen atoms were obtained from Δρ-maps; isotropic thermal parameters of the hydrogen atoms were taken as 1.5 times of the temperature factors for their parent atoms and the hydrogen atom positions were refined using a riding model. The refinement converged with an R = 0.0632, wR2 = 0.1616 with $w = 1/[\alpha^2(Fo^2) + 0.1210P^2 + 0.3139P]$, where $P = (Fo^2 + 2Fc^2)/3$, the empirical extinction correction coefficient g = 0.184(13)), and S = 1.072 (191 parameters); $\Delta\rho_{min}$ = -0.32 A^{-3}, $\Delta\rho_{max}$ = 0.35 $eÅ^3$. The atomic scattering factors were taken from SBELXL-93 [12]. The crystallographic data of **6c** are collected in Table 1.

Crystal X-ray analysis of **6d** and **8d**.

Preliminary data were obtained with a KM4 diffractometer equipped with a CCD detector for **6d** and **8d**; the accurate cell dimensions were determined by the least-squares refinement from the settings of 1200 reflections; the crystals (dimensions of 0.2 x 0.2 x 0.3 mm for **6d** and 0.1 x 0.2 x 0.3 mm. for **8d**) were applied to collect diffraction data on KM4 diffractometer by the ω scan technique using graphite monochromated MoKα radiation at room temperature. The data were collected for **6d** in the range [h:-16/17, k: -17/17, l: -19/19] while for **8d** in the range [h: -11/11, k: -9/8, l: -26/26]; no absorption correction was applied. For **6d** 28838 reflections were measured, of which 5517 reflections were considered to be observed with 0 < 20°; the corresponding data for **8d** were 15931 and 2983 reflections with 0 < 25°, respectively. The structures were solved using a direct method (SBELXTL-PC) [11]. E-map provided positions for all non-hydrogen atoms. The full-matrix least-squares refinement was carried out on $F^{2'}$s using anisotropic temperature factors for all non-hydrogen atoms were located geometrically, then the positions of the hydrogen atoms were refined in the riding model with isotropic thermal parameters taken as 1.5 times the temperature factors for their parent atoms. The refinement for **6d** converged with R = 0.0812, wR2 = 0.165 with $w = l/[\sigma^2(Fo^2) + 0.0336P^2 + 15.145P]$, where $P = (Fo^2 + 2Fc^2)/3$, the empirical extinction correction coefficient g = 0.0009(2), and S = 1.221 (758 parameters); $\Delta\rho_{min}$ = -0.296 $eÅ^3$, $\Delta\rho_{max}$ = 0.971 $eÅ^3$. Corresponding data for **8d** are: R = 0.0630, wR2 = 0.1778 with $w = 1/[\sigma^2(Fo^2) + 0.0527p^2 + 1.6376P]$, where $P = (Fo^2 + 2Fc^2)/3$, the empirical extinction correction coefficient g = 0.006(2), and S = 1.128 (227 parameters); $\Delta\rho_{min}$ = -0.460 $eÅ^3$, $\Delta\rho_{max}$ = 0.409 $eÅ^3$. The atomic scattering factors were taken from SBELXL-93 [12]. The crystallographic data of **6d** and **8d** are collected in Table 1.

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