Chemistry of Heterocyclic Compounds, Vol. 34, No. 3, 1998

HYDRAZONES OF α-PYRAZOLIDINYLACETOACETIC ESTER

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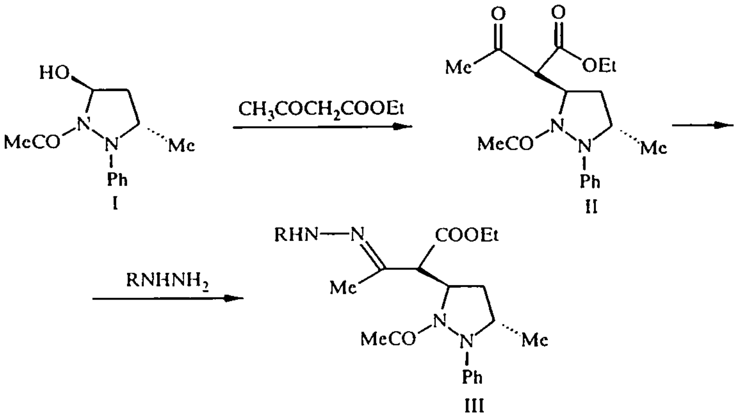
The p-nitrophenylhydrazones and acetylhydrazones of trans-α-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)-acetoacetic ester have been obtained in the form of a mixture of diastereomeric pairs of syn-isomers. Individual diastereomeric pairs that have been isolated do not undergo any tautomeric conversions in nonpolar solvents. Heterocyclization of these hydrazones is difficult.

We had shown in previous studies [1, 2] that 5-hydroxypyrazolidines I react readily with β-dicarbonyl compounds on an adsorbent surface without solvent, forming the corresponding multifunctional derivatives of pyrazolidine. However, any further application in synthesis is difficult, owing to the low yields and the laborious procedures needed to segregate the products of the solid-phase reactions, and also the instability of the β-dicarbonyl substituent in many of these compounds. Here we are reporting on an investigation of reactions of α-pyrazolidinyl-β-dicarbonyl compounds with hydrazine derivatives.

For these studies, we selected the α-pyrazolidinylacetoacetic ester II, which exhibits adequate activity in reactions of the carbonyl group with nucleophilic agents, and which is relatively resistant to decomposition under the conditions of its synthesis. The only isomer known, the trans-isomer, is formed on the surface of an adsorbent without solvent; as we had shown previously [2], the use of a polyamide in place of Al_2O_3 can increase the yield of compound II to 20%.



III a) R = MeCO; b) R = CHO; c) R = p-$NO_2C_6H_4$; d) R = C_6H_5CO;
e) R = $CONH_2$; f) R = $CSNH_2$; g) R = Ts

The lability of NH-free pyrazolidines predetermines instability of derivatives of 1-acylpyrazolidine in the synthesis when the acyl protection is removed, such conditions including the action of strong bases. We were not able to conduct the reaction of the α-pyrazolidinylacetoacetic ester with hydrazine; under these conditions, the original compound decomposes completely. In the case of phenylhydrazine, we observed severe tarring of the reaction mixture, so that we were unable to segregate or identify the reaction products. The interaction of compound II with p-nitrophenylhydrazine and the hydrazides of acids proceeds without any side processes, leading to the formation of mixtures of diastereomeric pairs (~ 1:1) of monosubstituted syn-hydrazones of the α-pyrazolidinylacetoacetic ester III. The syn-configuration of one of the diastereomeric pairs of the hydrazone

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0009-3122/98/3403-0278$20.00

TABLE 1. Bond Lengths in Molecule of IIIf (2)

Bond	*l*, Å	Bond	*l*, Å
$S_{(27)}—C_{(25)}$	1,693(3)	$C_{(3)}—C_{(4)}$	1,518(4)
$O_{(13)}—C_{(12)}$	1,224(3)	$C_{(4)}—C_{(5)}$	1,537(4)
$O_{(17)}—C_{(16)}$	1,217(3)	$C_{(5)}—C_{(15)}$	1,536(4)
$O_{(18)}—C_{(16)}$	1,321(3)	$C_{(6)}—C_{(11)}$	1,391(4)
$O_{(18)}—C_{(19)}$	1,463(3)	$C_{(6)}—C_{(7)}$	1,402(4)
$N_{(1)}—C_{(12)}$	1,368(3)	$C_{(7)}—C_{(8)}$	1,386(4)
$N_{(1)}—N_{(2)}$	1,430(3)	$C_{(8)}—C_{(9)}$	1,387(4)
$N_{(1)}—C_{(5)}$	1,483(3)	$C_{(9)}—C_{(10)}$	1,387(4)
$N_{(2)}—C_{(6)}$	1,423(3)	$C_{(10)}—C_{(11)}$	1,387(4)
$N_{(2)}—C_{(3)}$	1,489(3)	$C_{(12)}—C_{(14)}$	1,502(4)
$N_{(23)}—C_{(21)}$	1,288(3)	$C_{(15)}—C_{(21)}$	1,519(3)
$N_{(23)}—N_{(24)}$	1,384(3)	$C_{(15)}—C_{(16)}$	1,519(4)
$N_{(24)}—C_{(25)}$	1,369(3)	$C_{(19)}—C_{(20)}$	1,478(5)
$N_{(26)}—C_{(25)}$	1,315(4)	$C_{(21)}—C_{(22)}$	1,491(4)
$C_{(3)}—C_{(28)}$	1,511(4)		

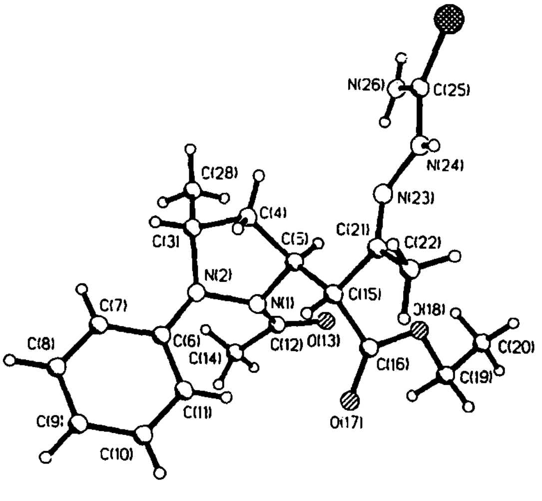

Fig. 1. General view of molecule of IIIf (2).

IIIf (2)* was established by x-ray diffraction studies (see Fig. 1 and Tables 1-4). In the molecule of compound IIIf (2), the pyrazolidine heterocycle has the conformation of a slightly distorted envelope (Table 3). The deviation of the $C_{(3)}$ atom from the $N_{(1)}N_{(2)}C_{(5)}C_{(4)}$ plane (planarity ±0.013 Å) is −0.493 Å. The dihedral angle with this plane, and also with a plane passing through the $N_{(2)}C_{(3)}C_{(4)}$ atoms, is 32.3°. The substituents in the heterocycle have a mutual trans-position, which reduces the steric nonvalence interaction between them (Fig. 1, Table 3). A similar conformation of the heterocycle and a similar orientation of the substituents were established previously [2, 3] in related molecules. The redistribution of bond lengths that is noted in the thioamide fragment of the molecule indicates conjugation in this fragment. The other values of the bond lengths and angles in the molecules of IIIf (2) coincide with those observed in substituted pyrazolidines in [2, 3] and are close to the standard values [4].

The formation of diastereomeric pairs is indicated by the NMR spectra, where doubling of these signals is observed. For the hydrazones IIIa, b, c, f, we were able to separate the diastereomeric pairs chromatographically. The characteristics and ratios of the isomers that were obtained are listed in Table 5, and the NMR data in Tables 6 and 7.

Interconversion of diastereomers in the α-pyrazolidinylacetoacetic ester and its hydrazones, which include three chiral centers, is directly related to the possibility of tautomeric conversions of the keto-enol type in these compounds. As we had

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*The diastereomeric pair with higher chromatographic mobility is indicated by (1), that with the lower mobility by (2).

TABLE 2. Bond Angles (deg) in Molecule of IIIf (2)

Angle	ω, deg	Angle	ω, deg
C$_{(16)}$—O$_{(18)}$—C$_{(19)}$	115,1(2)	C$_{(7)}$—C$_{(8)}$—C$_{(9)}$	120,2(3)
C$_{(12)}$—N$_{(1)}$—N$_{(2)}$	118,5(2)	C$_{(8)}$—C$_{(9)}$—C$_{(10)}$	119,0(3)
C$_{(12)}$—N$_{(1)}$—C$_{(5)}$	120,6(2)	C$_{(11)}$—C$_{(10)}$—C$_{(9)}$	121,5(3)
N$_{(2)}$—N$_{(1)}$—C$_{(5)}$	112,0(2)	C$_{(10}$—C$_{(11)}$—C$_{(6)}$	119,5(3)
C$_{(6)}$—N$_{(2)}$—N$_{(1)}$	116,7(2)	O$_{(13)}$—C$_{(12)}$—N$_{(1)}$	120,2(2)
C$_{(6)}$—N$_{(2)}$—C$_{(3)}$	117,5(2)	O$_{(13)}$—C$_{(12)}$—C$_{(14)}$	123,1(2)
N$_{(1)}$—N$_{(2)}$—C$_{(3)}$	104,7(2)	N$_{(1)}$—C$_{(12)}$—C$_{(14)}$	116,6(2)
C$_{(21)}$—N$_{(23)}$—N$_{(24)}$	118,2(2)	C$_{(21)}$—C$_{(15)}$—C$_{(16)}$	112,1(2)
C$_{(25)}$—N$_{(24)}$—N$_{(23)}$	117,2(2)	C$_{(21)}$—C$_{(15)}$—C$_{(5)}$	112,1(2)
N$_{(2)}$—C$_{(3)}$—C$_{(28)}$	110,1(2)	C$_{(16)}$—C$_{(15)}$—C$_{(5)}$	111,5(2)
N$_{(2)}$—C$_{(3)}$—C$_{(4)}$	104,0(2)	O$_{(17)}$—C$_{(16)}$—O$_{(18)}$	124,2(2)
C$_{(28)}$—C$_{(3)}$—C$_{(4)}$	113,3(3)	O$_{(17)}$—C$_{(16)}$—C$_{(15)}$	122,6(2)
C$_{(3)}$—C$_{(4)}$—C$_{(5)}$	105,3(2)	O$_{(18)}$—C$_{(16)}$—C$_{(15)}$	113,2(2)
N$_{(1)}$—C$_{(5)}$—C$_{(15)}$	112,5(2)	O$_{(18)}$—C$_{(19)}$—C$_{(20)}$	107,4(3)
N$_{(1)}$—C$_{(5)}$—C$_{(4)}$	102,9(2)	N$_{(23)}$—C$_{(21)}$—C$_{(22)}$	126,3(2)
C$_{(15)}$—C$_{(5)}$—C$_{(4)}$	111,8(2)	N$_{(23)}$—C$_{(21)}$—C$_{(15)}$	115,9(2)
C$_{(11)}$—C$_{(6)}$—C$_{(7)}$	119,2(2)	C$_{(22)}$—C$_{(21)}$—C$_{(15)}$	117,8(2)
C$_{(11)}$—C$_{(6)}$—N$_{(2)}$	123,9(2)	N$_{(26)}$—C$_{(25)}$—N$_{(24)}$	117,1(2)
C$_{(7)}$—C$_{(6)}$—N$_{(2)}$	116,9(2)	N$_{(26)}$—C$_{(25)}$—S$_{(27)}$	123,7(2)
C$_{(8)}$—C$_{(7)}$—C$_{(6)}$	120,6(3)	N$_{(24)}$—C$_{(25)}$—S$_{(27)}$	119,2(2)

TABLE 3. Principal Torsion Angles τ in Molecule of IIIf (2)

Angle	τ	Angle	τ
N$_{(1)}$—N$_{(2)}$—C$_{(3)}$—C$_{(4)}$	-32,6	C$_{(5)}$—C$_{(15)}$—C$_{(16)}$—O$_{(17)}$	-93,7
N$_{(2)}$—C$_{(3)}$—C$_{(4)}$—C$_{(5)}$	31,1	C$_{(19)}$—O$_{(18)}$—C$_{(16)}$—C$_{(15)}$	-169,0
C$_{(3)}$—C$_{(4)}$—C$_{(5)}$—N$_{(1)}$	-17,5	C$_{(5)}$—C$_{(15)}$—C$_{(21)}$—C$_{(22)}$	163,3
N$_{(2)}$—N$_{(1)}$—C$_{(5)}$—C$_{(4)}$	-2,9	C$_{(5)}$—C$_{(15)}$—C$_{(21)}$—N$_{(23)}$	-15,3
C$_{(5)}$—N$_{(1)}$—N$_{(2)}$—C$_{(3)}$	22,6	C$_{(16)}$—O$_{(18)}$—C$_{(19)}$—C$_{(20)}$	158,5
N$_{(1)}$—N$_{(2)}$—C$_{(6)}$—C$_{(7)}$	-178,1	O$_{(17)}$—C$_{(16)}$—O$_{(18)}$—C$_{(19)}$	10,3
C$_{(12)}$—N$_{(1)}$—N$_{(2)}$—C$_{(6)}$	103,0	C$_{(21)}$—C$_{(15)}$—C$_{(16)}$—O$_{(17)}$	139,6
N$_{(2)}$—N$_{(1)}$—C$_{(12)}$—O$_{(13)}$	161,2	N$_{(24)}$—N$_{(23)}$—C$_{(21)}$—C$_{(15)}$	175,5
N$_{(2)}$—N$_{(1)}$—C$_{(12)}$—C$_{(14)}$	-22,1	C$_{(21)}$—N$_{(23)}$—N$_{(24)}$—C$_{(25)}$	-173,5
C$_{(12)}$—N$_{(1)}$—C$_{(5)}$—C$_{(15)}$	-95,5	N$_{(24)}$—N$_{(23)}$—C$_{(21)}$—C$_{(22)}$	-2,9
N$_{(1)}$—C$_{(5)}$—C$_{(15)}$—C$_{(16)}$	51,4	N$_{(23)}$—N$_{(24)}$—C$_{(25)}$—N$_{(26)}$	-13,9
N$_{(1)}$—C$_{(5)}$—C$_{(15)}$—C$_{(21)}$	178,1	N$_{(23)}$—N$_{(24)}$—C$_{(25)}$—S$_{(27)}$	164,7

noted previously [2] in the case of the ketoester II in solution, enolization takes place, as evidenced by the fact that we could not distinguish any diastereomeric pairs in the NMR spectra. In the case of its hydrazones III, such hydrazone–enhydrazine conversion does not take place under these conditions; the individual diastereomeric pairs that were recovered are stable, and do not change into each other during storage. However, we did find that the isomer IIIa (1), when refluxed in isobutyl alcohol for an extended period, forms a mixture of diastereomeric pairs.

The data from NMR spectroscopy with the application of the NOE [nuclear Overhauser effect] for the individual diastereomeric pairs IIIb (1) and IIIb (2) also indicate the syn-configuration of the hydrazone fragment (Table 8). With saturation of the protons of the methyl group C=N bond, an NOE is observed on the protons of the NH and CHO groups; and conversely, with saturation of the protons of the NH and CHO groups, the effect is observed on the methyl group but is not observed on the proton in the α-position of the acetoacetic group.

The hydrazones III in solution are capable of forming both intermolecular and intramolecular hydrogen bonds. According to the IR spectroscopic data, in the tosylhydrazone IIIg, an intramolecular hydrogen bond is formed between the NH group of the hydrazine part of the molecule and the oxygen of the acetyl substituent of the pyrazolidine ring. In its spectra, when the CCl_4 solvent is replaced by THF, the shoulder on the absorption band of the amide group (1660 cm^{-1}) disappears, and the band of the NH group is shifted in its maximum from 3240 cm^{-1} to the region of 3310 cm^{-1}. Another fact that should be noted is that for the thiosemicarbazone, an intramolecular hydrogen bond is observed only in the isomer IIIf (1). According

TABLE 4. Coordinates ($\times 10^4$) and Isotropic-Equivalent (or Isotropic for H) Thermal Parameters of Atoms in Molecule of IIIf (2)

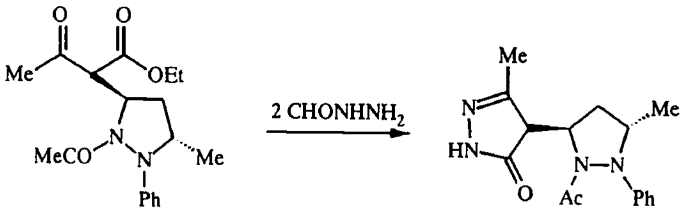
Atom	x	y	z	$U_{(eq)}$
1	2	3	4	5
$S_{(27)}$	2294(1)	922(1)	5711(1)	36(1)
$O_{(13)}$	-100(1)	-1673(2)	1366(1)	38(1)
$O_{(17)}$	838(1)	-192(2)	824(1)	43(1)
$O_{(18)}$	624(1)	956(2)	1708(1)	33(1)
$N_{(1)}$	729(1)	-2923(2)	1703(1)	24(1)
$N_{(2)}$	962(1)	-4300(2)	1790(1)	25(1)
$N_{(23)}$	1573(1)	-64(2)	3491(1)	26(1)
$N_{(24)}$	1892(1)	680(2)	4170(1)	27(1)
$N_{(26)}$	1342(1)	-409(3)	4713(1)	35(1)
$C_{(3)}$	1296(1)	-4494(3)	2653(1)	30(1)
$C_{(4)}$	1531(1)	-3055(3)	2954(2)	35(1)
$C_{(5)}$	1070(1)	-2042(3)	2395(1)	25(1)
$C_{(6)}$	1250(1)	-4665(3)	1307(1)	25(1)
$C_{(7)}$	1463(1)	-6028(3)	1373(2)	31(1)
$C_{(8)}$	1733(1)	-6482(3)	907(2)	36(1)
$C_{(9)}$	1783(1)	-5600(3)	357(2)	33(1)
$C_{(10)}$	1561(1)	-4262(3)	281(1)	30(1)
$C_{(11)}$	1298(1)	-3783(3)	752(1)	25(1)
$C_{(12)}$	136(1)	-2741(3)	1289(1)	28(1)
$C_{(14)}$	-192(1)	-3866(4)	716(2)	36(1)
$C_{(15)}$	1359(1)	-793(3)	2188(1)	25(1)
$C_{(16)}$	915(1)	20(3)	1499(1)	26(1)
$C_{(19)}$	119(1)	1579(4)	1060(2)	43(1)
$C_{(20)}$	-276(2)	2145(5)	1389(2)	62(1)
$C_{(21)}$	1690(1)	128(3)	2895(1)	24(1)
$C_{(22)}$	2124(1)	1134(3)	2844(2)	33(1)
$C_{(25)}$	1804(1)	358(3)	4821(1)	26(1)
$C_{(28)}$	895(2)	-5067(5)	2996(2)	58(1)
$H_{(3)}$	1644(12)	-5109(29)	2744(16)	27(7)
$H_{(41)}$	1921(13)	-2921(28)	2908(15)	29(7)
$H_{(42)}$	1623(16)	-2955(40)	3477(23)	66(11)
$H_{(5)}$	795(10)	-1744(25)	2583(13)	12(6)
$H_{(7)}$	1411(13)	-6680(33)	1732(17)	39(8)
$H_{(8)}$	1880(14)	-7458(39)	945(19)	55(9)
$H_{(9)}$	2001(14)	-5927(32)	32(18)	45(8)
$H_{(10)}$	1627(11)	-3613(27)	-56(15)	23(6)
$H_{(11)}$	1136(11)	-2886(31)	704(15)	27(7)
$H_{(141)}$	-157(16)	-4748(44)	953(22)	64(11)
$H_{(142)}$	21(20)	-3941(44)	373(25)	88(14)
$H_{(143)}$	-585(16)	-3563(34)	423(19)	48(9)
$H_{(15)}$	1672(11)	-1108(26)	2027(15)	24(7)

TABLE 4 (continued)

1	2	3	4	5
$H_{(191)}$	-79(15)	804(38)	658(21)	60(10)
$H_{(192)}$	295(16)	2303(43)	811(22)	70(11)
$H_{(201)}$	-634(15)	2591(35)	960(19)	52(9)
$H_{(202)}$	-372(16)	1350(41)	1671(22)	57(11)
$H_{(203)}$	-41(19)	2876(47)	1778(25)	83(13)
$H_{(221)}$	2514(17)	865(37)	3187(21)	55(10)
$H_{(222)}$	2102(15)	1212(34)	2302(22)	56(10)
$H_{(223)}$	2068(17)	1986(46)	3057(23)	73(12)
$H_{(24)}$	2218(15)	1128(33)	4248(18)	40(9)
$H_{(261)}$	1047(13)	-670(30)	4239(18)	31(7)
$H_{(262)}$	1216(14)	-528(35)	5070(20)	45(9)
$H_{(281)}$	705(19)	-5900(46)	2739(25)	78(13)
$H_{(282)}$	1144(15)	-5164(35)	3558(23)	55(9)
$H_{(283)}$	531(23)	-4515(51)	2875(28)	97(16)

to x-ray diffraction data on compound IIIf (2), intermolecular hydrogen bonds ($N_{(26)}-H_{(261)}...O_{(13)}$ ($-x$, y, $0.5 - z$) [$N_{(26)}...O_{(13)}$ 3.152(4), $N_{(26)}-H_{(261)}$ 0.92(3), $H_{(261)}...O_{(13)}$ 2.36(3) Å, angle $N_{(26)}-H_{(261)}...O_{(13)}$ 144(3)°] and $N_{(26)}-H_{(262)}...O_{(17)}$ (x, $-y$, $0.5 + z$) [$N_{(26)}...O_{(17)}$ 2.921(4), $N_{(26)}-H_{(262)}$ 0.86(3), $H_{(262)}...O_{(17)}$ 2.13(3) Å, angle $N_{(26)}-H_{(262)}...O_{(17)}$ 153(3)°] unite the molecules of the hydrazone IIIf into a crystal. For the molecules of IIIf (2), we did not detect any other shortened nonvalence intermolecular contacts in the crystalline state, i.e., lengths shorter than the sum of the van der Waals radii of the atoms [5].

It should be noted that the monosubstituted hydrazones III exhibit an unusually high stability for this class of compounds against intramolecular condensation resulting in pyrazolone derivatives. By the action of various reagents (inorganic acids and bases), we were likewise unable to cyclize the monosubstituted hydrazones III to the corresponding bis-heterocyclic compounds. The reaction mixtures contained only traces of the expected products of cyclization.



II

IV

The sole example of this sort of a quantitative conversion is the reaction of an α-pyrazolidinylacetoacetic ester with a twofold excess of formylhydrazine when heated for an extended period in alcohol solution, yielding only the one cyclic compound IV, which we had identified previously in [3].

EXPERIMENTAL

The IR spectra were measured in a UR-20 instrument in solutions of CCl_4 and CH_2Cl_2. The PMR and ^{13}C NMR spectra were measured in Bruker AC-200 and Varian VXR-400 instruments in chloroform solutions, with HMDS as an internal standard. For the experiments based on the NOE, we used the NOEDIF program [7]. Mass spectra were taken in a Kratos MS-890 instrument with direct introduction of the sample at temperatures close to the melting point, with ionization energy 70 eV.

The course of the reaction and the purities of the products were monitored by TLC on Silufol UV-254 plates in a 1/1 benzene/ethyl acetate system, development by iodine vapor and an alcoholic solution of iron(III) chloride. The compounds that were obtained were purified by high-efficiency flash chromatography on L 40/100 silica gel, and also by chromatography in a dry column on L 5/40 silica gel.

TABLE 5. Characteristics of Monosubstituted Hydrazones of α-Pyrazolidinylacetoacetic Ester III

Compound	Reaction time, h	mp, °C	R_f	Empirical formula	Found, % / Calculated, %			IR spectrum (CH_2Cl_2, CCl_4)	Mass spectrum, M^+, m/z	Yield, %
					C	H	N			
IIIa (1)	2 days*	145...147	0,25	$C_{20}H_{28}N_4O_4$	62,40 62,02	7,27 6,98	14,77 14,47	1610, 1680, 1740, 3380	388	46
IIIa (2)		158...160	0,15					1605, 1685, 1740, 3360		38
IIIb (1)	6	155...158	0,25	$C_{19}H_{26}N_4O_4$	60,58 61,00	7,05 7,00	15,16 15,00	1605, 1675, 1715, 1740, 3360		44
IIIb (2)		172...174	0,15					1605, 1670, 1715, 1740, 3200		30
IIIc (1)	5	208 (decomp.)	0,55	$C_{24}H_{29}N_5O_5$				1545, 1610, 1660, 1730, 3280	467	29
IIIc (2)		158...160	0,45					1550, 1605, 1675, 1730, 3330	467	54
IIId (1)	12	190...192	0,45	$C_{25}H_{30}N_4O_4$				1605, 1680, 1690 (sh), 1740, 3350, 3400	450	43
IIId (2)		135...137	0,30					1605, 1680, 1690 (sh), 1740, 3350, 3400		37
IIIe	1	113...115	0,15	$C_{19}H_{27}N_5O_4$	58,42 58,6	7,08 6,9	18,19 18,0	1600, 1685 (sh), 1695, 1740, 3390, 3420, 3520, 3540	389	93
IIIf (1)	6	147...150	0,60	$C_{19}H_{27}N_5O_3S$		6,79 6,7	16,89 17,3	1610, 1680, 1740, 3300 (bound), 3385, 3500, 3525		30
IIIf (2)		191 (decomp.)	0,40					1615, 1690, 1745, 3385, 3500, 3525		22
IIIg	5	89	0,45	$C_{25}H_{32}N_4O_3S$	59,98 60,0	6,35 6,4	11,19 11,2	1605, 1660 (sh), 1680, 1740, 3240 (bound), 3310 (free)		54

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*This reaction proceeds at room temperature, in the other cases upon refluxing in alcohol.

TABLE 6. PMR Spectra of Monosubstituted Hydrazones of α-Pyrazolidinylacetoacetic Ester III (δ, ppm)

Compound	5-H, m	α-CH, d	3-H, m	CH_3CO, s	4-H, m	3-CH_3, d	CH_3(Et), t	CH_2(Et), q	NH	$CH_3C=N$
IIIa (1)	4,95	3,37	4,14	2,42	1,95, 2,23	1,24	1,21	4,17	8,85	2,20
IIIa (2)	5,05	3,23	4,18	2,19	1,90, 2,10	1,25	1,33	4,24	9,48	1,92
IIIb (1)	5,05	3,36	4,15	2,05	1,90, 2,05	1,25	1,32	4,13	8,55	1,89
IIIb (2)	4,98	3,24	4,25	2,15	2,15, 2,20	1,28	1,21	4,22	8,65	1,95
IIIc (1)	4,88	3,40	4,12	2,02	2,14, 2,23	1,12	1,14	4,07	10,0	1,89
IIIc (2)	5,10	3,29	4,23	2,09	1,90, 2,02	1,25	1,27	4,14	10,0	1,96
IIId (1)	4,87	3,60	4,18	2,14	1,89, 2,20	1,18	1,19	4,11	9,14	2,00
IIId (2)	5,02	3,44	4,10	2,05	1,90...2,05	1,20	1,32	4,19	9,08	2,04
IIIe*	4,98 (5,19)	3,12 (3,05)	4,10...4,20	2,01 (1,98)	1,90...2,05	1,25 (1,18)	1,15 (1,25)	4,00...4,10	8,63 (8,75)	1,86 (1,83)
IIIf (1)	5,25	3,00	4,07	1,97	2,04, 2,15	1,30	1,16	4,08	8,50	1,82
IIIf (2)	4,95	3,17	4,06	2,00	1,89, 2,00	1,18	1,25	4,15	8,50	1,89
IIIg *	4,65 (4,83)	3,34 (3,11)	3,99...4,09	2,27 (2,39)	1,60...2,20	1,14 (1,11)	1,18 (1,24)	4,06...4,12	7,90 (7,74)	1,96 (2,02)

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*For compounds IIIe and IIIg, the spectra were obtained on a mixture of the diastereomeric pairs.

TABLE 7. ^{13}C NMR Spectra of Monosubstituted Hydrazones of α-Pyrazolidinylacetoacetic Ester III (δ, ppm)

	IIIa(1)	IIIa(2)	IIIb(1)	IIIb(2)	IIIc(1)	IIIc (2)	IIId (1)	IIId (2)	IIIe	IIIf (1)	IIIf (2)	IIIg[*3]
$\underline{C}H_3CO$[*]	20,50	20,43	21,23	21,35	21,18	21,45	21,43	20,94	21,18 (21,20)	21,50	21,25	21,37
C_4	38,23	38,40	38,17	38,43	38,30	38,38	38,45	37,97	38,02 (38,72)	38,73	38,02	37,73
C_5	60,15	59,05	58,97	60,03	58,85	60,50	60,05	58,68	58,37 (58,83)	57,60	58,95	60,04
C_3	55,40	55,97	55,97	55,60	56,05	55,80	55,62	55,78	55,11 (56,04)	54,83	55,98	55,65
3-CH_3	14,03	15,02	15,05	14,05	14,05	14,13	14,05	13,80	14,08 (14,67)	14,55	14,78	13,93
$CH_3\underline{C}O$[*2]	173,00	173,97	176,12	176,38	176,13	176,40	176,20	175,93	176,40 (176,58)	176,75	176,40	176,10
α-CH	61,20	61,55	61,72	61,40	61,60	61,35	61,20	61,50	61,36 (61,51)	61,63	61,93	61,23
$EtO\underline{C}O$[*2]	169,90	169,77	169,75	169,90	170,20	170,33	170,17	169,80	169,69 (169,89)	168,85	169,32	169,90
CH_2(Et)	60,70	60,28	60,47	60,58	60,35	60,70	60,70	60,30	59,99 (60,38)	59,90	60,43	61,05
CH_3(Et)	12,87	13,82	13,93	13,35	13,87	12,55	13,08	13,60	13,90 (13,99)	13,92	13,98	13,46
CH_3CN[*]	19,70	19,86	20,00	19,90	19,95	19,90	19,65	19,50	20,11 (20,11)	21,13	20,05	21,15
C=N	149,72	149,90	150,00	150,45	149,95	150,15	149,35	149,70	149,98 (150,03)	150,02	149,95	149,45
Ph C^o	114,60	114,35	114,42	114,63	114,35	114,80	115,05	114,30	114,29 (113,32)	112,80	114,42	115,16
C^p	120,40	121,27	121,40	121,55	121,30	121,75	121,67	121,30	121,03 (121,30)	121,30	121,58	121,73
C^m	129,00	129,12	129,27	129,15	129,15	129,22	128,60	128,45	128,21 (129,20)	129,47	129,37	129,19
C^i	147,65	146,47	149,37	149,63	144,13	146,30	146,82	146,95	144,79 (144,52)	146,38	147,17	143,56
R	21,20 176,12	21,15 176,00	166,17	165,53	112,00 125,80 140,22 144,13	111,95 126,05 140,22 144,13	127,25 129,34 133,72 144,00	127,30 129,10 131,96 149,70	157,85 (158,07)	179,30	179,37	19,17 128,03 129,47 135,90 153,60

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[*], [*2] Assignment of these signals in the spectrum may be reversed.

[*3] Data are for the spectrum of the predominant diastereomeric pair.

TABLE 8. Magnitude of NOE (η, %) for Compound IIIb

Signal observed	IIIb (1)			IIIb (2)		
	Protons irradiated			Protons irradiated		
	CH_3CN	NH	α-CH	CH_3CN	NH	α-CH
CH_3CN	*	4,0	—	*	4,2	—
NH	1,2	*	—	3,3	*	—
α-CH	1,5	—	*	2,5*	—	*
HCO	1,8	3,5	—	0,9	4,7	—

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*It was difficult to determine an accurate value of η, since the signal of the CH_3CN of the isomer IIIb (2) is overlapped by the signal of 4-H in the pyrazolidine ring.

X-Ray Structure Study. The crystals of compound IIIf (2) are monoclinic; at $-80°C$, $a = 25.072(10)$, $b = 9.630(3)$, $c = 18.813(6)$ Å, $\beta = 115.08(3)°$, $V = 4114(2)$ Å^3, $d_{calc} = 1.310$ g/cm^3, Z = 8, space group C2/c. The cell constants and the intensities of 3709 reflections were measured in a Syntex $P2_1$ four-circle automatic diffractometer (λMoKα, graphite monochromator, $\theta/2\theta$ scanning to $\theta_{max} = 27°$). The structure was deciphered by the direct method, defining all nonhydrogen atoms, and was refined by full-matrix LMS in the anisotropic approximation for the nonhydrogen atoms. All hydrogen atoms were defined objectively by Fourier difference syntheses and were refined isotropically. The final divergence factors were R = 0.052 based on 2629 independent reflections with $I > 3\sigma(I)$ and $wR_2 = 0.138$ based on 3626 reflections. All calculations were performed by the programs SHELXTL PLUS and SHELXTL-93 (PC version). The coordinates and the isotropically equivalent thermal parameters of the nonhydrogen atoms (or isotropic for H) are listed in Table 4.

Monosubstituted Hydrazones of α-(1-Acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)acetoacetic Ester (IIIa, b, c, d, f, g). A mixture of α-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)acetoacetic ester II and a half-molar equivalent quantity of the appropriate monosubstituted hydrazine was refluxed in absolute ethyl ether. The reaction was monitored by TLC. After completion of the reaction, the solvent was removed under vacuum, and the dry residue was washed with water to remove excess hydrazine, dried in a desiccator over $CaCl_2$, and chromatographed in a dry column or by the flash chromatography method.

Semicarbazone of α-(1-Acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)acetoacetic Ester (IIIe). To a solution of 0.11 g (1.98 mmoles) of potassium hydroxide and 0.29 g (1.98 mmoles) of semicarbazide hydrochloride in 10 ml of absolute ether, a solution of 0.33 g (0.99 mole) of α-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)acetoacetic ester II in 8 ml of absolute ether was added while refluxing the solution. Then the solvent was driven off, and the residue was washed with water and ether and then recrystallized from a mixture of chloroform and ether.

3-Methyl-4-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)-5-pyrazolone (IV). A mixture of 0.30 g (0.90 mmole) of α-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)acetoacetic ester (II) and 0.12 g (2.0 mmoles) of formylhydrazine in absolute alcohol was refluxed for 10 h. The solvent was removed under vacuum, the residue was water-washed to remove excess hydrazine, and then was dried over $CaCl_2$. The product was chromatographed in a dry column with SiO_2 in a benzene/ethyl acetate system, with a solvent gradient of 1:1 to 1:5. Yield 0.11 g (41%).

The authors wish to express their appreciation to the Russian Fundamental Research Fund (Grants 96-03-32507 and 96-03-33783a) for financial support of this work.

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