Synthesis of derivatives of 2-hydroxyimino- and 2-alkoxyimino-3-(acylhydrazono)butanoic acids

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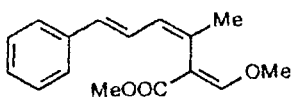
Esters and *N*-methylamides of 2-hydroxyimino- and 2-alkoxyimino-3-(acylhydrazono)-butanoic acids were synthesized by condensation of acyl hydrazines with the corresponding alkyl 2-hydroxyimino- and 2-alkoxyimino-3-oxobutanoates and *N*-methyl-2-methoxyimino-3-oxobutanamide. The compounds obtained are analogs of strobilurins, fungicidal antibiotics.

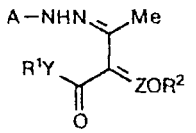
Key words: esters and amides of 2-hydroxyimino-3-oxobutanoic and 2-alkoxyimino-3-oxobutanoic acids, hydrazones; strobilurin analogs.

Strobilurin A (**1**) is an antibiotic of high fungicidal activity. But it is light-sensitive, which significantly limits the area of its application.[1] There have been synthesized a large number of structural analogs of strobilurin A that have various biological activities and are more stable and promising as agrochemical preparations against a broad spectrum of plant diseases. Esters and amides of aryl- and hetarylacetic acids bearing the methoxymethylene or methoxyimino group in the α-position are the major strobilurin analogs studied.[2–4]

Acylhydrazones of esters and amides of 2-alkoxymethylene- and 2-alkoxyimino-3-oxobutanoic acids (**2**) are structurally close to strobilurin and therefore can also exhibit similar biological activity.



1



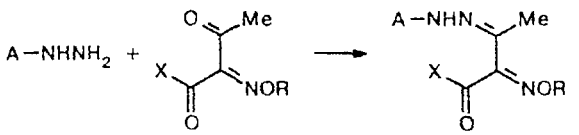
2

A = Acyl; Z = CH, N; Y = O, NR^3, R^1 = Alk; R^2, R^3 = H, Alk

Earlier, we showed[5] that hydrazones of ethyl 2-(ethoxymethylene)acetoacetate could not be prepared by the condensation of the ester with substituted hydrazines. However, derivatives of 2-(hydroxyimino)acetoacetic acid smoothly react with various acyl hydrazines to give the corresponding hydrazones (Scheme 1).

Condensation of acyl hydrazines **3a—f** with esters **4—9** or amide **10** was carried out by heating equimolar amounts of the reagents in ethanol (thiosemicarbazones were obtained in an ethanol—water mixture). Some hydrazones (compounds **12c,d** and **16f**) were not formed under these conditions. For this reason they were synthesized in the presence of hydrochloric acid as a catalyst, which, in most cases, allowed the reaction to be completed after 20 min against one hour in usual practice. The fact that the yields were not always close to quantitative may be explained by the high solubility of the target products in the reaction mixture and losses during recrystallization. The melting points and yields of hydrazones **11—17** are given in Table 1.

Scheme 1



3a—f **4—10** **11—17**

3a—f: A = PhCO (**a**); *p*-BrC_6H_4CO (**b**); *m*-BrC_6H_4CO (**c**);

(**d**); H_2NCS (**e**); EtOCO (**f**).

X = MeO, R = H (**4**, **11a—e**); Me (**5**, **12a—f**); Et (**6**, **13a—f**);
X = EtO, R = H (**7**, **14a—e**); Me (**8**, **15a—f**); Et (**9**, **16a—f**);
X = MeNH, R = Me (**10**, **17a—e**).

As can be seen from the above scheme, the condensation in both neutral and acidic media involves the keto group of derivatives of acetoacetic acid rather than the azomethine group. Under these conditions, the hydrazones formed do not undergo cyclization involving the ester or amide group to give pyrazolidine derivatives.

Alkyl 2-alkoxyimino-3-oxobutanoates (**5**, **6**, **8**, and **9**) were obtained by nitrosation of ethyl and methyl acetoacetates with sodium nitrite in acetic acid followed by alkylation of hydroxyimino derivatives **4** and **7** obtained with dimethyl or diethyl sulfate (Scheme 2).

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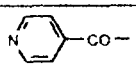
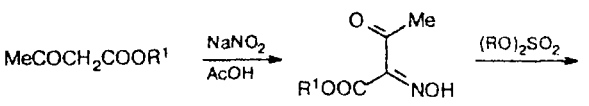
Table 1. Melting points and yields of acylhydrazones **11—17**

Compound	X	R	A[a]	Yield (%)		M.p./°C
				Without catalyst	With catalyst	
11a	MeO	H	PhCO	23.5	—	155—158
11b	MeO	H	4-BrC_6H_4CO	44	—	182—186 (decomp.)
11c	MeO	H	3-BrC_6H_4CO	22	—	184—186
11d	MeO	H	4-pyCO	43	—	170—172 (decomp.)
11e	MeO	H	$H_2NC(=S)$	66	—	180—182 (decomp.)
12a	MeO	Me	PhCO	6	47	164—166
12b	MeO	Me	4-BrC_6H_4CO	89	—	157—160
12c	MeO	Me	3-BrC_6H_4CO	0	98	179—181
12d	MeO	Me	4-pyCO	0	91	201—205 (decomp.)
12e	MeO	Me	$H_2NC(=S)$	20.5	—	206—211 (decomp.)
12f	MeO	Me	EtOCO	65	—	126—128
13a	MeO	Et	PhCO	—	71	155—157
13b	MeO	Et	4-BrC_6H_4CO	—	79	157—159
13c	MeO	Et	3-BrC_6H_4CO	—	75	162—164
13d	MeO	Et	4-pyCO	—	41	164—167
13e	MeO	Et	$H_2NC(=S)$	79	—	195—200[b]
13f	MeO	Et	EtOCO	—	40	119—121
14a	EtO	H	PhCO	79	—	180—181
14b	EtO	H	4-BrC_6H_4CO	66	—	179—182
14c	EtO	H	3-BrC_6H_4CO	44	—	127—128
14d	EtO	H	4-pyCO	57	—	181—182
14e	EtO	H	$H_2NC(=S)$	69	—	181—183 (decomp.)
15a	EtO	Me	PhCO	63	—	120—122
15b	EtO	Me	4-BrC_6H_4CO	58	—	144—146
15c	EtO	Me	3-BrC_6H_4CO	64	—	119—122
15d	EtO	Me	4-pyCO	59	—	186—188
15e	EtO	Me	$H_2NC(=S)$	35	—	215—218 (decomp.)
15f	EtO	Me	EtOCO	60	—	104—105
16a	EtO	Et	PhCO	—	61	135—139
16b	EtO	Et	4-BrC_6H_4CO	—	28	130—132
16c	EtO	Et	3-BrC_6H_4CO	—	70	127—131
16d	EtO	Et	4-pyCO	—	63	158—160
16e	EtO	Et	$H_2NC(=S)$	33	—	decomp. >180
16f	EtO	Et	EtOCO	0	60	95—97
17a	MeNH	Me	PhCO	—	13	188—192
17b	MeNH	Me	4-BrC_6H_4CO	—	41	216—218 (decomp.)
17c	MeNH	Me	3-BrC_6H_4CO	—	59	234—236 (decomp.)
17d	MeNH	Me	4-pyCO	—	22	213—216 (decomp.)
17e	MeNH	Me	$H_2NC(=S)$	—	61	174—178 (decomp.)

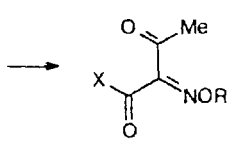
[a] 4-pyCO =  . [b] In a sealed capillary.

Scheme 2



R^1 = Me, Et

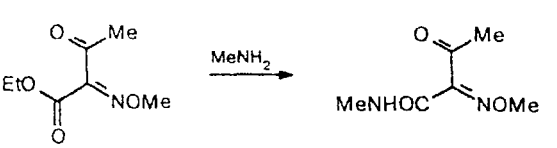
4: R^1 = Me,
7: R^1 = Et



5, 6, 8, 9

N-Methyl-2-methoxyimino-3-oxobutanamide (**10**) was obtained by aminolysis of ethyl 2-methoxyimino-3-oxobutanoate (**8**) (Scheme 3).

Scheme 3



8 **10**

Table 2. ^{1}H NMR and IR spectroscopy data of acylhydrazones **11—17**

Compound	^{1}H NMR, δ (*J*/Hz)	IR, ν/cm^{-1}
11a	2.15 (s, 3 H, MeC=); 3.65 (s, 3 H, COOMe); 7.50 (m, 3 H, arom.); 7.80 (d, 2 H, arom.); 10.90 (s, 1 H, NH); 12.10 (s, 1 H, OH)	3200 (NH, OH), 1760 (C=O est.), 1630 (amide I)
11b	2.15 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 7.70 (s, 4 H, arom.); 11.00 (br.s, 1 H, NH); 12.20 (s, 1 H, OH)	3210 (NH, OH), 1760 (C=O est.), 1670 (amide I)
11c	2.15 (s, 3 H, MeC=); 3.70 (br.s, 3 H, COOMe); 7.60—7.90 (m, 4 H, arom.); 11.00 (br.s, 1 H, NH); 12.20 (s, 1 H, OH)	3330, 3230 (NH, OH), 1770 (C=O est.), 1670 (amide I)
11d	2.15 (s, 3 H, MeC=); 3.60 (br.s, 3 H, COOMe); 7.60 (br.s, 2 H, arom.); 8.70 (d, 2 H, arom., *J* = 4.5); 11.20 (br.s, 1 H, NH); 12.20 (s, 1 H, OH)	3230 (NH, OH), 1760 (C=O est.), 1670 (amide I)
11e	2.15 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 7.00, 8.35 (both br.s, each 1 H, NH_2); 10.60 (s, 1 H, NH); 12.20 (s, 1 H, OH)	3460, 3300, 3210 (NH, OH), 1740 (C=O)
12a	2.15 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 3.95 (s, 3 H, NOMe); 7.50 (m, 3 H, arom.); 7.80 (d, 2 H, arom., *J* = 7); 11.00 (br.s, 1 H, NH)	3200 (NH), 1760 (C=O est.), 1690 (amide I)
12b	2.15 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 3.95 (s, 3 H, NOMe); 7.70 (s, 4 H, arom.); 11.10 (br.s, 1 H, NH)	3200 (NH), 1760 (C=O est.), 1670 (amide I)
12c	2.15 (s, 3 H, MeC=); 3.70 (br.s, 3 H, COOMe); 4.00 (s, 3 H, NOMe); 7.30 (t, 1 H, arom., *J* = 7.9); 7.65 (dt, 1 H, arom., *J* = 7.9, *J* = 1.7); 7.75 (dt, 1 H, arom., *J* = 7.9, *J* = 1.7); 7.95 (t, 1 H, arom., *J* = 1.7); 9.15 (br.s, 1 H, NH)	1770 (C=O est.), 1670 (amide I)
12d	2.15 (s, 3 H, MeC=); 3.60 (br.s, 3 H, COOMe); 3.95 (s, 3 H, NOMe); 7.60 (br.s, 2 H, arom.); 8.70 (d, 2 H, arom., *J* = 4.5); 11.30 (br.s, 1 H, NH)	3100 (NH), 1760 (C=O est.), 1690 (amide I)
12e	2.15 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 3.95 (s, 3 H, NOMe); 7.10, 8.40 (both br.s, each 1 H, NH_2); 10.65 (br.s, 1 H, NH)	3450, 3300, 3200 (NH), 1750 (C=O)
12f	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.05 (s, 3 H, MeC=); 3.75 (s, 3 H, COOMe); 3.95 (s, 3 H, NOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 10.40 (br.s, 1 H, NH)	3270 (NH), 1770 (C=O est.), 1730 (amide I)
13a	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.20 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 7.40—7.60 (m, 3 H, arom.); 7.80 (d, 2 H, arom., *J* = 7); 10.95 (s, 1 H, NH)	3270, 3240 (NH), 1750 (C=O est.), 1670 (amide I)
13b	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.20 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 4.20 (q, 2 H, CH_2); 7.70 (s, 4 H, arom.); 11.05 (br. s, 1 H, NH)	3200 (NH), 1740 (C=O est.), 1660 (amide I)
13c	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.20 (s, 3 H, MeC=); 3.70 (s, 3 H, COOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 7.45 (t, 1 H, arom., *J* = 8); 7.75 (d, 2 H, arom., *J* = 8); 7.90 (s, 1 H, arom.); 11.05 (s, 1 H, NH)	3270, 3240 (NH), 1760 (C=O est.), 1670 (amide I)
13d	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.20 (s, 3 H, MeC=); 3.60 (br.s, 3 H, COOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 7.60 (br.s, 2 H, arom.); 8.70 (d, 2 H, arom., *J* = 4.5); 11.30 (br.s, 1 H, NH)	3100 (NH), 1760 (C=O est.), 1690 (amide I)
13e	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.15 (s, 3 H, MeC=); 3.80 (s, 3 H, COOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 7.00, 8.40 (both br.s, each 1 H, NH_2); 10.65 (br. s, 1 H, NH)	3460, 3300, 3210 (NH), 1750 (C=O)
13f	1.25 (2 t, 6 H, CH_2<u>Me</u>, *J* = 7); 2.05 (s, 3 H, MeC=); 3.75 (s, 3 H, COOMe); 4.20 (2 q, 4 H, CH_2, *J* = 7); 10.35 (s, 1 H, NH)	3260, 3180 (NH), 1770 (C=O est.), 1710 (amide I)
14a	1.20 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.15 (s, 3 H, MeC=); 4.15 (q, 2 H, CH_2, *J* = 7); 7.40—7.60 (m, 3 H, arom.); 7.80 (d, 2 H, arom., *J* = 8); 10.85 (s, 1 H, NH); 12.10 (s, 1 H, OH)	3200 br (NH, OH), 1770 (C=O), 1650 (amide I)
14b	1.25 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.15 (s, 3 H, MeC=); 4.15 (q, 2 H, CH_2, *J* = 7); 7.70 (s, 4 H, arom.); 11.00 (br.s, 1 H, NH); 12.10 (s, 1 H, OH)	3300 br (NH, OH), 1730 (C=O est.), 1690 (amide I)
14c	1.20 (t, 3 H, CH_2<u>Me</u>, *J* = 7); 2.15 (s, 3 H, MeC=); 4.15 (q, 2 H, CH_2, *J* = 7); 7.60—7.90 (m, 4 H, arom.); 11.00 (br.s, 1 H, NH); 12.10 (s, 1 H, OH)	3300 br (NH, OH), 1770 (C=O est.), 1645 (amide I)

(to be continued)

Table 2 (*continued*)

Compound	^{1}H NMR, δ (*J*/Hz)	IR, ν/cm^{-1}
14d	1.15 (br. s, 3 H, CH_2Me); 2.15 (s, 3 H, MeC=); 4.10 (br.s, 2 H, CH_2); 7.60 (br.s, 2 H, arom.); 8.70 (d, 2 H, arom., *J* = 7); 11.20 (br.s, 1 H, NH); 12.10 (br.s, 1 H, OH)	3230 (NH, OH), 1750 (C=O est.), 1700 (amide I)
14e	1.25 (t, 3 H, CH_2Me, *J* = 7), 2.15 (s, 3 H, MeC=); 4.30 (q, 2 H, CH_2, *J* = 7); 6.90, 8.40 (both br.s, each 1 H, NH_2); 10.60 (s, 1 H, NH); 12.15 (s, 1 H, OH)	3450, 3300, 3230 (NH), 1750 (C=O)
15a	1.20 (br.s, 3 H, CH_2Me); 2.15 (s, 3 H, MeC=); 3.93 (s, 3 H, NOMe); 4.20 (br.s, 2 H, CH_2); 7.40—7.60 (m, 3 H, arom.); 7.80 (br.s, 2 H, arom.); 11.10 (s, 1 H, NH)	3370 (NH), 1730 (C=O est.), 1700 (amide I)
15b	1.20 (t, 3 H, CH_2Me, *J* = 7); 2.15 (s, 3 H, MeC=); 3.95 (s, 3 H, NOMe); 4.20 (q, 2 H, CH_2, *J* = 7); 7.70 (s, 4 H, arom.); 11.05 (br.s, 1 H, NH)	3370 br, 3210 br (NH), 1730 (C=O est.), 1710 (amide I)
15c	1.20 (br.t, 3 H, CH_2Me, *J* = 7); 2.15 (s, 3 H, MeC=); 3.95 (s, 3 H, NOMe); 4.20 (br.q, 2 H, CH_2, *J* = 7); 7.45 (t, 1 H, arom., *J* = 7); 7.75 (d, 2 H, arom., *J* = 7); 7.90 (s, 1 H, arom.); 11.10 (s, 1 H, NH)	3230 br (NH), 1760 (C=O est.), 1680 (amide I)
15d	1.15 (br.s, 3 H, CH_2Me); 2.15 (s, 3 H, MeC=); 3.95 (s, 3 H, NOMe); 4.10 (br.s, 2 H, CH_2); 7.65 (br.s, 2 H, arom.); 8.70 (d, 2 H, arom., *J* = 4.5); 11.30 (br.s, 1 H, NH)	1750 (C=O est.), 1685 (amide I)
15e	1.25 (t, 3 H, CH_2Me, *J* = 7); 2.10 (s, 3 H, MeC=); 3.95 (s, 3 H, NOMe); 4.30 (q, 2 H, CH_2, *J* = 7); 7.00, 8.40 (both br.s, each 1 H, NH_2); 10.70 (s, 1 H, NH)	3480, 3300, 3200 (NH), 1775 (C=O)
15f	1.25 (2 t, 6 H, 2 CH_2Me, *J* = 7); 2.00 (s, 3 H, MeC=); 3.95 (s, 3 H, NOMe); 4.20 (2 q, 4 H, 2 CH_2, *J* = 7); 10.35 (br. s, 1 H, NH)	3300, 3200 (NH), 1760 (C=O est.), 1715 (amide I)
16a	1.20 (m, 6 H, 2 CH_2Me); 2.20 (s, 3 H, MeC=); 4.20 (m, 4 H, 2 CH_2); 7.40—7.60 (m, 3 H, arom.); 7.80 (d, 2 H, arom., *J* = 7); 10.95 (s, 1 H, NH)	3250 (NH), 1755 (C=O est.), 1675 (amide I)
16b	1.20 (br.s, 3 H, $COOCH_2$Me,); 1.30 (t, 3 H, $NOCH_2$Me, *J* = 7); 2.15 (s, 3 H, MeC=); 4.20 (br.s, 2 H, $COOCH_2$); 4.25 (q, 2 H, $NOCH_2$, *J* = 7); 7.56—7.73 (A_2B_2-system, 4 H, arom.); 9.00 (br. s, 1 H, NH)	3240 br (NH), 1770 (C=O est.), 1670 (amide I)
16c	1.20 (2 t, 6 H, 2 CH_2Me, *J* = 7); 2.20 (s, 3 H, MeC=); 4.20 (2 q, 4 H, 2 CH_2, *J* = 7); 7.45 (t, 1 H, arom., *J* = 7); 7.75 (d, 2 H, arom., *J* = 7); 7.95 (s, 1 H, arom.); 11.10 (s, 1 H, NH)	3230 (NH), 1750 (C=O est.), 1675 (amide I)
16d	1.15 (br.s, 3 H, $COOCH_2$Me); 1.20 (t, 3 H, $NOCH_2$Me, *J* = 7); 2.20 (s, 3 H, MeC=); 4.10 (br.s, 2 H, $COOCH_2$); 4.20 (q, 2 H, $NOCH_2$, *J* = 7); 7.65 (br.s, 2 H, arom.); 8.80 (d, 2 H, arom., *J* = 4.5); 11.25 (s, 1 H, NH)	1760 (C=O est.), 1680 (amide I)
16e	1.15 (2 t, 6 H, 2 CH_2Me, *J* = 7); 2.15 (s, 3 H, MeC=); 4.25 (2 q, 4 H, 2 CH_2, *J* = 7); 7.20, 8.65 (both br.s, each 1 H, NH_2); 10.70 (s, 1 H, NH)	3400, 3300, 3200 (NH), 1745 (C=O)
16f	1.30 (m, 9 H, 3 CH_2Me); 2.02 (s, 3 H, MeC=); 4.25 (2 q, 4 H, 2 CH_2, *J* = 7); 4.40 (q, 2 H, CH_2, *J* = 7); 7.65 (br. s, 2 H, arom.); 7.90 (br.s, 1 H, NH)	3260 (NH), 1770 (C=O est.), 1725 (amide I)
17a	2.11 (s, 3 H, MeC=); 2.60 (br.s, 3 H, NMe); 3.88 (s, 3 H, NOMe); 7.40—7.60 (m, 3 H, arom., *J* = 7); 7.79 (d, 2 H, arom., *J* = 7); 8.15 (br.s, 1 H, NHMe); 10.95 (br.s, 1 H, NHN=)	3370, 3205 (NH), 1680, 1645 (amide I)
17b	2.11 (s, 3 H, MeC=); 2.55 (br.s, 3 H, NMe); 3.88 (s, 3 H, NOMe); 7.70 (br.s, 4 H, arom.); 8.15 (br.s, 1 H, NHMe); 11.10 (br.s, 1 H, NHN=)	3315, 3220 (NH), 1680, 1650 (amide I)
17c	2.12 (s, 3 H, MeC=); 2.61 (br.s, 3 H, NMe); 3.89 (s, 3 H, NOMe); 7.40 (t, 1 H, arom., *J* = 8); 7.70 (d, 1 H, arom., *J* = 8); 7.80 (d, 1 H, arom.; *J* = 8), 7.97 (s, 1 H, apom); 8.15 (br.s, 1 H, NHMe); 11.05 (br.s, 1 H, NHN=)	3340, 3225 (NH), 1670, 1650 (amide I)

(*to be continued*)

Table 2 (*continued*)

Compound	^{1}H NMR, δ (*J*/Hz)	IR, ν/cm^{-1}
17d	2.08 (br.s, 3 H, MeC=); 2.40/2.65* (br.s, 3 H, NMe); 3.87 (br. s, 3 H, NOMe); 7.56/7.75 (br.s, 2 H, arom.); 8.66/8.75 (br.s, 2 H, arom.); 8.05/8.20 (br.s, 1 H, NHMe); 11.30 (br.s, 1 H, NHN=)	3390, 3200 (NH), 1700, 1645 (amide I)
17e	2.07 (br.s, 3 H, MeC=); 2.64 (d, 3 H, NMe, *J* = 4.7); 3.88 (s, 3 H, NOMe); 6.95, 8.64 (both br.s, each 1 H, NH_2); 8.20 (q, 1 H, NHMe, *J* = 4.7); 10.80 (br.s, 1 H, NHN=)	3300, 3170 (NH), 1640 (amide I)

* Signals for two geometric isomers are separated by a solidus; the intensity ratio ~1 : 1.

Table 3. Data of elemental analysis of acylhydrazones **11**—**17**

Compound	Found / Calculated (%) C	H	N	Molecular formula
11a	54.81 / 54.75	4.91 / 4.98	15.91 / 15.96	$C_{12}H_{13}N_3O_4$
11b	42.24 / 42.13	3.64 / 3.54	12.11 / 12.28	$C_{12}H_{12}BrN_3O_4$
11c	42.30 / 42.13	3.48 / 3.54	12.40 / 12.28	$C_{12}H_{12}BrN_3O_4$
11d	49.73 / 50.00	4.45 / 4.58	21.06 / 21.20	$C_{11}H_{12}N_4O_4$
11e	33.11 / 33.02	4.70 / 4.62	25.69 / 25.67	$C_6H_{10}N_4O_3S$
12a	56.12 / 56.31	5.58 / 5.45	15.21 / 15.15	$C_{13}H_{15}N_3O_4$
12b	43.75 / 43.84	3.81 / 3.96	11.72 / 11.80	$C_{13}H_{14}BrN_3O_4$
12c	44.41 / 43.84	3.88 / 3.96	12.03 / 11.80	$C_{13}H_{14}BrN_3O_4$
12d	52.12 / 51.80	5.24 / 5.07	20.05 / 20.14	$C_{12}H_{14}N_4O_4$
12e	36.74 / 36.20	5.25 / 5.21	24.14 / 24.12	$C_7H_{12}N_4O_3S$
12f	43.60 / 44.08	6.07 / 6.16	17.18 / 17.13	$C_9H_{15}N_3O_5$
13a	57.69 / 57.72	5.80 / 5.88	13.90 / 14.42	$C_{14}H_{17}N_3O_4$
13b	46.10 / 45.42	4.26 / 4.36	11.40 / 11.35	$C_{14}H_{16}BrN_3O_4$
13c	45.14 / 45.42	4.15 / 4.36	11.18 / 11.35	$C_{14}H_{16}BrN_3O_4$
13d	54.33 / 53.42	5.60 / 5.52	19.38 / 19.17	$C_{13}H_{16}N_4O_4$
13e	39.60 / 39.01	5.72 / 5.73	23.16 / 22.73	$C_8H_{14}N_4O_3S$
13f	47.05 / 46.33	6.65 / 6.60	16.22 / 16.21	$C_{10}H_{17}N_3O_5$
14a	56.48 / 56.31	5.59 / 5.45	15.38 / 15.15	$C_{13}H_{15}N_3O_4$
14b	44.89 / 43.84	3.89 / 3.96	11.50 / 11.80	$C_{13}H_{14}BrN_3O_4$
14c	44.50 / 43.84	3.99 / 3.96	12.14 / 11.80	$C_{13}H_{14}BrN_3O_4$
14d	52.01 / 51.80	5.15 / 5.07	20.00 / 20.14	$C_{12}H_{14}N_4O_4$
14e	35.70 / 36.20	5.18 / 5.21	24.55 / 24.12	$C_7H_{12}N_4O_3S$
15a	57.72 / 57.72	5.77 / 5.88	14.41 / 14.42	$C_{14}H_{17}N_3O_4$
15b	46.10 / 45.42	4.37 / 4.36	11.42 / 11.35	$C_{14}H_{16}BrN_3O_4$
15c	45.64 / 45.42	4.28 / 4.36	11.52 / 11.35	$C_{14}H_{16}BrN_3O_4$
15d	53.90 / 53.42	5.60 / 5.52	18.90 / 19.17	$C_{13}H_{16}N_4O_4$
15e	39.48 / 39.01	5.82 / 5.73	22.57 / 22.73	$C_8H_{14}N_4O_3S$
15f	46.28 / 46.33	6.70 / 6.61	16.19 / 16.21	$C_{10}H_{17}N_3O_5$
16a	58.74 / 59.01	6.16 / 6.27	13.77 / 13.76	$C_{15}H_{19}N_3O_4$
16b	47.59 / 46.89	4.90 / 4.72	10.78 / 10.94	$C_{15}H_{18}BrN_3O_4$
16c	47.97 / 46.89	4.81 / 4.72	10.69 / 10.94	$C_{15}H_{18}BrN_3O_4$
16d	55.01 / 54.90	5.92 / 5.92	17.89 / 18.29	$C_{14}H_{18}N_4O_4$
16e	42.56 / 41.52	6.29 / 6.20	21.05 / 21.52	$C_9H_{16}N_4O_3S$
16f	48.44 / 48.34	7.12 / 7.01	15.48 / 15.38	$C_{11}H_{19}N_3O_5$
17a	57.24 / 56.51	5.83 / 5.84	20.81 / 20.28	$C_{13}H_{16}N_4O_3$
17b	43.07 / 43.96	4.21 / 4.26	15.97 / 15.77	$C_{13}H_{15}BrN_4O_3$
17c	44.50 / 43.96	4.42 / 4.26	15.54 / 15.77	$C_{13}H_{15}BrN_4O_3$
17d	52.91 / 51.98	5.42 / 5.45	25.36 / 25.26	$C_{12}H_{15}N_5O_3$
17e	36.64 / 36.35	5.76 / 5.67	30.28 / 30.28	$C_7H_{13}N_5O_2S$

Experimental

IR spectra were recorded on an IKS-29 instrument in Vaseline oil for all compounds except for **6** and **10** (thin film). ^{1}H NMR spectra were recorded on a Bruker AC-200 instrument (200 MHz) in DMSO-d_6 (in $CDCl_3$ for compounds **12c** and **16b**).

Methyl and ethyl 2-(hydroxyimino)acetoacetates (4 and 7) were synthesized by nitrosation of the corresponding alkyl acetoacetates.[6,7] **Alkyl 2-(methoxyimino)acetoacetates (5, 8)** and **ethyl 2-(ethoxyimino)acetoacetate (9)** were obtained by alkylation of esters **4** and **7** with dimethyl and diethyl sulfate, respectively.[6,7]

Methyl 2-ethoxyimino-3-oxobutanoate (6). Diethyl sulfate (21 g, 0.136 mol) was added with stirring to a suspension of methyl α-(hydroxyimino)acetoacetate (**4**) (18.9 g, 0.13 mol) and finely pulverized anhydrous K_2CO_3 (35 g, 0.255 mol) in 103 mL of acetone. The reaction mixture was stirred at ~20 °C for 2 h. After addition of water (1 L), the products were twice extracted with $CHCl_3$ (100 and 50 mL). The extract was dried over $MgSO_4$, and the solvent was removed to give ester **6** (17.3 g, 77%), n_D^{20} 1.4370. IR, ν/cm^{-1}: 1765 (C=O est.), 1710 (C=O ket.), 1615 (C=N).

***N*-Methyl-2-methoxyimino-3-oxobutanamide (10).** A 30% aqueous solution of $MeNH_2$ (20 mL) was added to a solution of ethyl α-(methoxyimino)acetoacetate (**7**) (10.5 g, 66 mmol) in 40 mL of THF. The reaction mixture was allowed to stand at ~20 °C for a week. Concentration of the solution gave *N*-methyl-2-methoxyimino-3-oxobutanamide **10** (9.4 g, 98%). IR, ν/cm^{-1}: 3300 (NH), 1690 (C=O ket.), 1660 (amide I), 1605 (C=N).

Condensation of methyl 2-methoxyimino-3-oxobutanoate (5) with benzohydrazide (3a). *A* (without a catalyst). Ester **5** (1 g, 6.29 mmol) and benzohydrazide (**3a**) (0.86 g, 6.29 mmol) were dissolved in 5 mL of EtOH. The reaction mixture was refluxed for 1 h and cooled. The crystals that formed were filtered off and recrystallized from EtOH to give methyl 2-methoxyimino-3-(benzoylhydrazono)butanoate **12a** (0.1 g, 6%).

***B* (with a catalyst).** The reaction was carried out with the same amounts of the reagents, but one drop of conc. HCl was added. The reaction mixture was refluxed for 20 min and cooled. The crystals that formed were filtered off and recrystallized from EtOH to give hydrazone **12a** (0.8 g, 47%).

Condensation of compounds **4—10** with other acyl hydrazines, except for thiosemicarbazide, was carried out in a similar way.

Condensation of methyl 2-methoxyimino-3-oxobutanoate (5) with thiosemicarbazide (3e). Boiling solutions of ester **5** (1 g, 6.29 mmol) in 3 mL of EtOH and thiosemicarbazide (0.57 g, 6.29 mmol) in 3 mL of water were mixed and refluxed with stirring for 30 min. The reaction mixture was then cooled, and the precipitate that formed was filtered off and washed with hot water and EtOH to give methyl 2-methoxyimino-3-oxobutanoate thiosemicarbazone **12e** (0.3 g, 21%).

Condensation of compounds **4—10** with thiosemicarbazide (**3e**) was carried out in a similar way.

Melting points and yields of hydrazones **11—17** are given in Table 1. IR and ^{1}H NMR spectral characteristics are summarized in Table 2. Data of elemental analysis are listed in Table 3.

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