1,3-Dipolar cycloaddition of cyclic α-methoxynitrones, derivatives of 2*H*-imidazole 1-oxide and 4*H*-imidazole 3-oxide

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The reactions of cyclic aldo- and α-methoxynitrones of the 2*H*-imidazole-1-oxide and 4*H*-imidazole 3-oxide series with isocyanates, phenyl isothiocyanate, *N*-phenylmaleimide, and dimethyl acetylenedicarboxylate were studied. The reactions give the corresponding 1,3-dipolar cycloaddition products. 2,2-Dimethyl-4-phenyl-2*H*-imidazole 1-oxide does not enter into a similar reaction with isocyanates or phenyl isothiocyanate.

Key words: nitrones, α-methoxynitrones, imidate *N*-oxides, 2*H*-imidazole 1-oxides, 4*H*-imidazole 3-oxides, 1,3-dipolar cycloaddition

1,3-Dipolar cycloaddition of nitrones is widely used in organic chemistry as a method for designing diverse heterocyclic systems; in particular, for the preparation of analogs of natural products.[1—3] To continue research into the properties of conjugated cyclic nitrones (2*H*- and 4*H*-imidazole *N*-oxides[4—9]), we studied[10] the reactions of cyclic aldo- and α-methoxynitrones of the 2*H*-imidazole 1-oxide and 4*H*-imidazole 3-oxide series with dipolarophiles containing C=N, C=C, and C≡C bonds. It should be noted that only three examples of 1,3-dipolar cycloaddition to 2*H*-imidazole *N*-oxides[11] and no data on the reactions of 4*H*-imidazole *N*-oxides with dipolarophiles have been reported to date. Known examples of 1,3-dipolar cycloaddition of α-alkoxynitrones are limited to the reactions of ethyl *N*-methylbenzimidate *N*-oxide and derivatives of 4,5-dihydrooxazole *N*-oxide.[12—15]

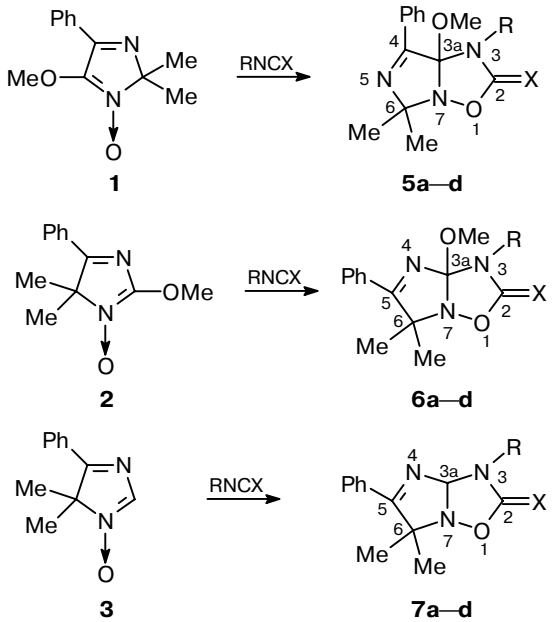
According to the published data, the reactivity of nitrones in 1,3-dipolar addition should be interpreted with allowance made for both the interaction of the dipole HOMO with the dipolarophile LUMO and the interaction of the dipole LUMO with the dipolarophile HOMO; for different dipolarophiles, either one of these interactions or both of them play the crucial role.[16] The order of conjugation of C=N bonds in the 2*H*-imidazole 1-oxide and 4*H*-imidazole 3-oxide molecules has, apparently, a substantial influence on the positions of the frontier orbitals; this is manifested, in particular, as a marked difference between their electrochemical oxidation potentials, which are equal to ~2 V and ~1.3 V *vs.* a saturated calomel electrode for 2*H*-imidazole 1-oxides and 4*H*-imidazole 3-oxides, respectively.[17,18] The introduction of a methoxy group to the α-carbon atom of the nitrone group increases the HOMO energy.[13,14] Thus, it could be expected that the reactivities of the nitrones studied can be appreciably different and can depend on the dipolarophile structure.

The purpose of this work is to study 1,3-dipolar cycloaddition of cyclic nitrones to isocyanates and isothiocyanates.

Results and Discussion

Cyclic α-methoxynitrones **1** and **2** react with isocyanates and isothiocyanates at ~25 °C giving rise to 1,3-dipolar addition products **5** and **6** (Scheme 1). Under the same conditions, a similar reaction of

Scheme 1



R = Ph (**a**, **b**), $ClCH_2CH_2$ (**c**), α-naphthyl (**d**);
X = O (**a**, **c**, **d**), S (**b**).

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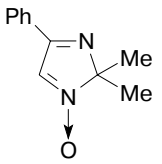
Table 1. Reactions of α-methoxynitrones **1**, **2** and aldonitrones **3**, **4a** with dipolarophiles at 25 °C in CH_2Cl_2

Dipolarophile	**1**			**2**			**3**			**4a**		
	I	II	III	I	II	III	I	II	III	I	II	III
PhNCO	**5a**	72	90	**6a**	0.08	70	**7a**	1	70	No reaction	—	—
PhNCS	**5b**	240	70	**6b**	5	70	**7b**[a]	24	95	No reaction	—	—
$ClCH_2CH_2NCO$	**5c**	120	60	**6c**	14	70	**7c**	336	70	No reaction	—	—
α-Naphthyl isocyanate	**5d**	72	90	**6d**	0.08	70	**7d**	1	70	No reaction	—	—
N-Phenylmaleimide[b]	**8**	24	70	**9**	504	40	**10**	24	70	**11a**	24	70

Note. Concentration of compounds **1**—**4a** was 0.2 mol L^{-1}. I is the reaction product; II is the reaction time/h; III is the yield (%).
[a] Without a solvent.
[b] The reactant concentrations were 1 mol L^{-1}.

aldonitrone **3** proceeds much more slowly than that of substrate **2**, while aldonitrone **4a** does not react at all (Table 1). Characteristics of the 1,3-cycloaddition products are listed in Table 2.



4a

The reactivity of nitrones in 1,3-dipolar cycloaddition increases when an alkoxyl substituent has been introduced in the α-position of the nitrone group.[14] The addition of isothiocyanates to nitrones can involve both the C=N and the C=S bond; in the case of 3-imidazoline 3-oxides containing electron-withdrawing substituents in position 1 of the heterocycle, addition at the C=S bond is the predominant reaction route.[19,20] In the reactions of compounds **1**, **2**, and **3** with PhNCS, only addition products at the C=N bond were isolated.

Cycloadducts **5**, **6**, and **7** are stable colorless crystalline compounds. Their structure is confirmed by the presence of absorption bands due to the carbonyl group of the oxadiazolidinone ring (1780—1750 cm^{-1}) in their IR spectra (*cf.* Refs. 13, 21) and by the double set of signals present in 3 : 7 ratio in the ^1H and ^{13}C NMR spectra of cycloadduct **5d** (Tables 3, 4), resulting from the pyramidal inversion of the N atom attached to the O atom of the oxadiazolidinone ring, slow on the NMR time scale (*cf.* Ref. 13).

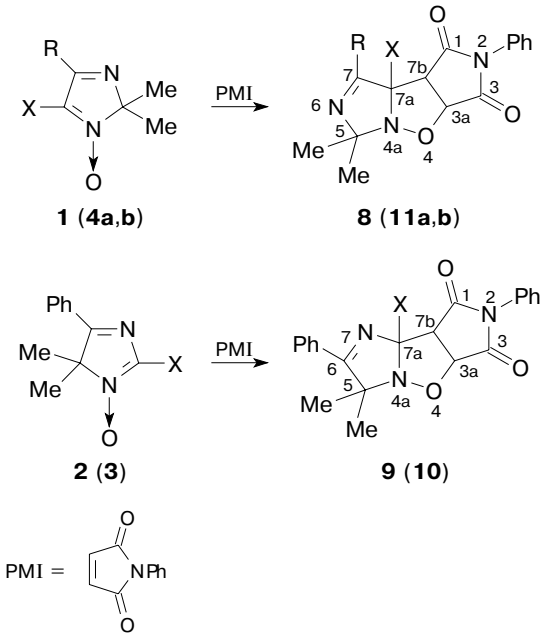
For the same reason, signals of the methyl and methoxy groups in the ^1H NMR spectrum of adduct **6d** recorded at 25 °C are markedly broadened, and the signals of the carbonyl and methoxy-group carbon atoms in the ^{13}C NMR spectrum are totally absent. The spectra of this compound recorded at −50 °C contain signals for two invertomers in 1 : 3 ratio. It is of interest that the signal of the azomethine carbon atom in the ^{13}C NMR spectra of compounds **5** is shifted upfield by 15—17 ppm with respect to the corresponding signal in the spectra of compounds **6** and **7**. This is consistent with the earlier data for 2,2- and 5,5-dialkoxy-substituted 2,5-dihydroimidazoles.[10]

Unlike isocyanates and isothiocyanates, *N*-phenylmaleimide (PMI) and dimethyl acetylenedicarboxylate (DMAD) react with all nitrones **1**—**4** at ~25 °C; the reactions of DMAD proceed at approximately equal rates, while for PMI, the reaction with α-methoxynitrone **2** is much slower than those with nitrones **1**, **3**, and **4**.

The reactions of compounds **1**, **2**, **3**, and **4a**,**b** with *N*-phenylmaleimide afford 3a,4a,7a,7b-tetrahydro-4-oxa-triazacyclopenta[*a*]pentalene-1,3-diones **8**, **9**, **10**, and **11a**,**b**, respectively (Scheme 2), which are colorless crystalline compounds whose IR spectra contain characteristic bands for the vibrations of the carbonyl groups of the pyrrolidine-1,3-dione ring (1796 and 1720—1724 cm^{-1}). The structures of these products are confirmed by the presence of absorption in the phenylimine region (240—250 nm) in the UV spectra of compounds **8**—**11a**.

The ^1H NMR spectra of cycloadducts **8** and **9** exhibit two, while those of compounds **10** and **11** exhibit three multiplets due to the methine protons at about 3.9—5.6 ppm. It is of interest that the spin-spin coupling constant for the pyrrolidine-1,3-dione ring

Scheme 2



1 (**4a**,**b**) **8** (**11a**,**b**)

2 (**3**) **9** (**10**)

Table 2. Characteristics of the compounds synthesized

Compound	Yield (%)	M.p. /°C	IR (KBr), ν/cm^{-1}	UV (EtOH), λ_{max}/nm (log ε)	Found / Calculated (%) C	H	N	Other	Molecular formula
5a	90	95—97	1620 (C=N); 1780 (C=O); 2845 (OMe)	253.1 (4.10)	67.94 67.64	5.68 5.68	12.54 12.46	—	$C_{19}H_{19}N_3O_3$
5b	70	117—119	1612 (C=N); 2830 (OMe)	248 (4.40)	64.86 64.57	5.52 5.42	11.96 11.89	9.20 [a] 9.07	$C_{19}H_{19}N_3O_2S$
5c	60	73—75	1625 (C=N); 1780 (C=O); 2835 (OMe)	248.6 (4.86)	55.95 55.64	5.80 5.60	13.00 12.98	11.00 [b] 10.99	$C_{15}H_{18}ClN_3O_3$
5d	90	122—125	1620 (C=N); 1770 (C=O); 2835 (OMe)	222.9 (4.43); 255.9 (4.22)	71.36 71.30	5.53 5.46	10.89 10.85	—	$C_{23}H_{21}N_3O_2$
6a	70	107—108	1610 (C=N); 1770 (C=O); 2850 (OMe)	233.8 (4.23)	67.96 67.64	5.82 5.68	12.56 12.46	—	$C_{19}H_{19}N_3O_3$
6b	70	82—85	1620 (C=N); 2850 (OMe)	250 sh (KBr)	64.50 64.57	5.36 5.42	11.80 11.89	9.30 [a] 9.07	$C_{19}H_{12}N_3O_2S$
6c	70	81—83	1620 (C=N); 1770 (C=O); 2845 (OMe)	249.6 (4.11)	55.40 55.64	5.48 5.60	12.96 12.98	11.00 [b] 10.95	$C_{15}H_{18}ClN_3O_3$
6d	90	144—146	1610 (C=N); 1780 (C=O); 2845 (OMe)	255 (KBr)	71.10 71.30	5.58 5.46	10.77 10.85	—	$C_{23}H_{21}N_3O_3$
7a	90	104—105	1640 (Ph—C=N); 1750 (C=O);	236.9 (4.33)	70.83 70.34	5.76 5.52	13.64 13.67	—	$C_{18}H_{17}N_3O_3$
7b	95	111—115	1620 (Ph—C=N)	248.6 (4.42)	67.08 66.85	5.26 5.30	12.97 12.99	—	$C_{18}H_{17}N_3OS$
7c	80	93—95	1610 (C=N); 1770 (C=O)	245.7 (4.12)	57.20 57.24	5.56 5.49	14.31 14.30	12.17 [b] 12.07	$C_{14}H_{16}ClN_3O_2$
7d	95	164—166	1620 (C=N); 1770 (C=O)	247 (4.24); 285 (4.03)	74.39 73.93	5.40 5.36	11.74 11.76	—	$C_{22}H_{19}N_3O_3$
8	70	200—202	1783 w. 1724 (C=O); 1616 (C=N); 2837 (OMe)	250 (3.82)	67.69 67.51	5.51 5.41	10.82 10.74	—	$C_{22}H_{21}N_3O_4$
9	40	190—193	1796 w; 1731 (C=O); 1597 (C=N); 2831 (OMe)	246 (4.00)	67.36 67.51	5.68 5.41	10.80 10.74	—	$C_{22}H_{21}N_3O_4$
10	70	210—211	1788 w; 1721 (C=O); 1607 (C=N)	241 (3.94)	69.75 69.79	4.87 5.30	11.41 11.63	—	$C_{21}H_{19}N_3O_3$
11a	80	200—210 (decomp.)	1796 w; 1721 (C=O); 1625 (C=N)	243 (4.22)	69.90 69.79	5.40 5.30	11.68 11.63	—	$C_{21}H_{19}N_3O_3$
11b	80	188—190	1796 w; 1721 (C=O); 1622 (C=N); 3058 (H—C=N); 2831 (OMe)	232 (3.99)	59.67 59.64	5.07 5.30	16.23 16.37	—	$C_{17}H_{18}N_4O_4$
12	90	87—91	1624 (C=N); 1751, 1731 (C=O); 1650 (C=C); 2834 (OMe)	245.7 (4.25)	60.54 59.99	5.62 5.59	7.74 7.77	—	$C_{18}H_{20}N_2O_6$
13	60	72—74	1607 (C=N); 1754; 1725; (C=O); 1659 (C=C); 2836; 2855 (OMe)[c]	249.6 (4.16)	59.92 59.99	5.37 5.59	7.43 7.77	—	$C_{18}H_{20}N_2O_6$
14	90	195—213	1670; 1750 (C=O); 1605 (C=N); 2870 (OMe); 3220 (N—H)	227.2 (4.10); 291.9 (4.20); 357.9 (4.11); 265 (4.13)[d]; 356 (3.52)[d]	61.69 61.81	5.52 5.49	8.30 8.48	—	$C_{17}H_{17}N_2O_5$
15	40	175—198 (decomp.)	1620 (C=N); 1700; 1737 (C=O); 3240 (N—H)	205 (4.26); 248.6 (4.00); 360.5 (4.00)	61.52 61.81	5.56 5.49	8.40 8.48	—	$C_{17}H_{17}N_3O_5$
18	40	130—132	1705, 1725 (C=O); 1595 (C=N); 2835 (OMe)	300 (3.69); 247 (3.05); 242 (3.05)	62.47 62.49	5.15 5.24	7.25 7.29	—	$C_{20}H_{20}N_2O_6$

[a] S.
[b] Cl.
[c] The IR spectrum was recorded in $CHCl_3$.
[d] The UV spectrum was recorded in a EtOH—H_2O mixture (1 : 1).

protons (7.5—8.5 Hz) is much greater than the coupling constant for the protons at C(7a) and C(7b) (0—1.5 Hz).

The reactions of compounds **1**—**3** and **4a** with DMAD (Scheme 3) are rather vigorous and, at reactant concentrations of >0.5 mol L^{-1}, it results in substantial warming-up and resinification of the reaction mixture. In the case of α-methoxynitrones **1** and **2**, this reaction affords isomeric imidazoisoxazoles **12** and **13**, similarly to the

Table 3. ^{1}H NMR spectra of cycloadducts **5—7**

Compound	Solvent	δ			
		Me_{gem} (both s, each 3 H)	OMe (s, 3 H or CH, s, 1 H)	N=C—Ph	N—R
5a	CD_3OD	1.63, 1.68	3.62	7.14, 7.30, 7.65 (all m, 4 H, 4 H and 2 H)	
5b	$CDCl_3$	1.61, 1.67	3.56	7.03, 7.20, 7.51 (all m, 4 H, 4 H and 2 H)	
5c	$CDCl_3$	1.45, 1.57	3.39	7.45, 8.02 (both m, 3 H and 2 H)	3.22, 3.44 (both m, 2 H, CH_2CH_2)
5d[a]	$(CD_3)_2CO$	1.70 (1.68), 1.83 (1.72)	3.62 (3.34)	7.32, 7.57 (both m, 3 H and 2 H)	6.68—7.8 (m, 7 H)
6a	$CDCl_3$	1.68, 1.70	3.47	7.45, 7.86 (both m, 6 H and 4 H)	
6b	$CDCl_3$	1.72, 1.75	3.50	7.49, 7.90 (both m, 3 H and 2 H)	7.50—7.62 (m, 5 H)
6c	$CDCl_3$	1.58, 1.64	3.42	7.46, 7.85 (both m, 3 H and 2 H)	3.78—3.55 (m, 4 H, CH_2CH_2)
6d[a,b]	$CDCl_3$	1.72, 1.79, (1.84)	3.43, (3.65)	7.55, 8.00 (both m, 3 H and 2 H)	7.35—8.23 (m, 7 H)
7a	CD_3OD	1.59, 1.74	7.10 (s, 1 H, CH)	7.54 (m, 10 H)	
7b	$CDCl_3$ + CD_3OD	1.57, 1.84	6.88 (s, 1 H, CH)	7.52, 7.85 (both m, 6 H and 4 H)	
7c	$CDCl_3$	1.46, 1.66	6.42 (s, 1 H, CH)	7.42, 7.74 (both m, 3 H and 2 H)	3.83 (m, 4 H, CH_2CH_2)
7d	$CDCl_3$	1.53, 1.82	6.65 (s, 1 H, CH)	7.49, 7.90 (both m, 3 H and 2 H)	7.36—8.13 (m, 7 H)

[a] The signals for the minor invertomer are given in parentheses.
[b] The spectra were recorded at −50 °C.

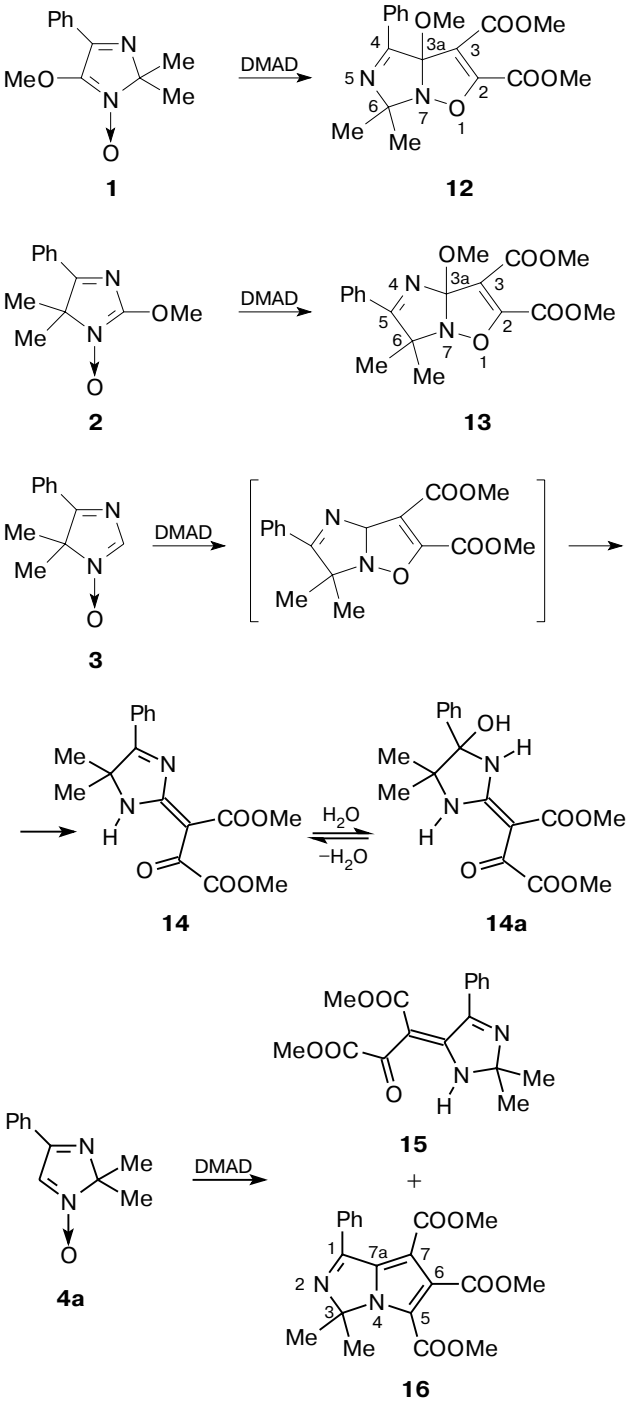
reaction reported for 4,5-dimethyl-2,2-diphenyl-2*H*-imidazole 1-oxide.[11]

The ^{1}H NMR spectra of the prepared compounds exhibit, apart from the two multiplets for protons of the phenylimine fragment, two singlets for the geminal methyl groups and three singlets for the methoxy groups, which differ markedly in chemical shift, obviously, due to the anisotropic influence of the benzene ring (Table 5).

A similar reaction of aldonitrone **3** is accompanied by opening of the isoxazole ring giving rise to enamino ketone **14** (*cf.* Ref. 11 for 4-methyl-2,2-diphenyl-2*H*-imidazole 1-oxide).

Product **14** can undergo easy reversible addition of an H_2O molecule to give covalent hydrate **14a**. Thus the intensity of the long-wavelength absorption maxima at

Scheme 3



391 and 357 nm in the UV spectrum of compound **14** markedly decreases when an ethanol—water mixture (1 : 1) is used instead of neat ethanol, and the presence of a small amount of water in deuterioacetone induces quantitative transformation of enamino ketone **14** into a covalent hydrate over a period of several days. Simultaneously, the singlet at 1.85 ppm due to the geminal methyl groups of compound **14** disappears, and two

Table 4. ^{13}C NMR spectra of cycloadducts **5—7**

Compound	Solvent	δ							
		Me_{gem}	OMe	$C(Me)_2$	C=O (C=S)	C(3a)	C=N	N=C—Ph	N—R
5a	CD_3OD	23.0, 23.0	51.0	95.1	162.9	114.7	157.1	131.3 (C_i); 130.3 (C_o); 130.3 (C_m); 132.4 (C_p)	134.3 (C_i); 129.0 (C_o); 129.8 (C_m); 130.3 (C_p)
5b	$CDCl_3$	23.0, 29.3	50.6	95.0	185.5	116.1	159.8	129.3 (C_i); 128.9 (C_o); 129.0 (C_m); 130.9 (C_p)	34.1 (C_i); 127.6 (C_o); 128.3 (C_m); 129.3 (C_p)
5c	$CDCl_3$	22.3, 29.3	49.9	95.0	160.5	125.0	155.7	131.0 (C_i); 128.2 (C_o); 128.7 (C_m); 131.7 (C_p)	39.6, 42.9
5d[a]	$(CD_3)_2CO$	23.0 (22.5), 30.0 (29.2)	50.5 (51.0)	94.0 (93.0)	161.5 (160.0)	114.2 (114.0)	161.5 (160.0)	130.2 (131.2) (C_i, Ph); 121.5 (124.0); 124.9 (124.4); 126.0 (126.6); 127.7 (128.0); 127.9 (126.9); 127.9 (128.3); 128.4 (128.4); 128.5 (128.6); 128.6 (129.3); 129.4 (130.0); 130.0 (130.7)	131.4 (133.9) (C_i, naphthyl);
6a	$CDCl_3$	21.0, 27.8	51.0	77.5	152.7	124.1	178.9	130.4 (C_i); 128.8 (C_o); 128.8 (C_m); 131.8 (C_p)	134.1 (C_i); 123.2 (C_o); 128.5 (C_m); 126.4 (C_p)
6b	$CDCl_3$	21.5, 27.6	51.5	78.0	184.3	123.5	179.3	130.0 (C_i); 128.7 (C_o); 129.0 (C_m); 132.1 (C_p)	134.6 (C_i); 126.6 (C_o); 128.8 (C_m); 127.5 (C_p)
6c	$CDCl_3$	20.8, 27.8	50.8	77.1	155.1	127.7	179.4	130.5 (C_i); 128.5 (C_o); 128.6 (C_m); 131.9 (C_p)	40.7, 42.7
6d[a,b]	$CDCl_3$	21.0, 27.6	52.7	76.2	153.2	125.1	178.4	130.5 (C_i); 128.6 (C_o); 128.8 (C_m); 132.2 (C_p)	134.1 (C_i); 122.2, 125.1, 125.4, 126.2, 127.0, 128.2, 128.3, 129.4, 130.0
7a	CD_3OD	21.1, 25.5	—	78.5	154.0	101.7	179.6	132.2 (C_i); 129.8 (C_o); 130.2 (C_m); 132.7 (C_p)	137.5 (C_i); 121.8 (C_o); 129.7 (C_m); 126.7 (C_p)
7b	$CDCl_3$ + CD_3OD	20.2, 24.9	—	77.7	181.5	102.7	177.7	129.7 (C_i); 131.3 (C_o); 128.0 (C_m); 128.1 (C_p)	135.9 (C_i); 127.7 (C_o); 128.6 (C_m); 127.7 (C_p)
7c	$CDCl_3$	20.4, 25.5	—	76.1	154.5	99.9	177.2	130.5 (C_i); 128.7 (C_o); 128.4 (C_m); 131.2 (C_p)	41.2, 44.4
7d	$CDCl_3$	20.8, 25.4	—	77.1	153.7	101.8	177.4	130.8 (C_i, Ph); 134.5 (C_i, naphthyl); 122.4, 125.4, 126.4, 126.7, 127.1, 128.4, 128.6, 129.4, 130.1, 130.7, 131.4	

[a] The signals for the minor invertomer are given in parentheses.
[b] The spectra were recorded at −50 °C; for the ^{13}C NMR spectrum, only the signals of the major inveromer are given.

singlets for nonequivalent methyl groups with chemical shifts of 0.81 and 1.58 ppm, typical of covalent hydrates of 4*H*-imidazole *N*-oxides[22] and of 4-hydroxy-5,5-dimethyl-1-methoxy-4-phenylimidazolidin-2-one,[10] appear instead; finally, the signal for the *ortho*-protons of the phenyl groups shifts uplfield by 0.63 ppm. Chromatography of compound **14a** is accompanied by elimination of a water molecule.

In the reaction of compound **4a** with DMAD, apart from enamino ketone **15**, a colorless crystalline product was isolated; according to spectroscopic data, this product complied with structure **16**. The structure ascribed to this compound is confirmed by the absence of bands for NH or OH groups in the region of 3000—3700 cm^{-1} in its IR spectrum and by the presence of absorption maxima at 302, 247, and 242 nm in the UV spectrum. The ^1H NMR spectrum of compound **16** exhibits signals for three methoxycarbonyl groups (see Table 4); the region of the ^{13}C NMR spectrum typical of olefins or aromatic compounds (δ 100—140) contains, in addition to the signals of the phenyl group, four signals for carbon atoms at 107.2, 121.5, 131.4, and 139.2 ppm. The mass spectrum of this compound shows a molecular ion with m/z 384. These data are consistent with the results of ebullioscopic measurement of the molecular mass (found, 362 in $CHCl_3$), and the results of elemental analysis correspond to the molecular formula $C_{20}H_{20}N_2O_6$. Based on these results, the product in question was identified as trimethyl 3,3-dimethyl-1-phenyl-3*H*-pyrrolo[1,2-*c*]imidazole-5,6,7-tricarboxylate **16**.

Enamino ketone **15** does not react with DMAD under reaction conditions, while the reaction of nitrone **4a** with DMAD gives both products in approximately equal amounts, irrespective of the content of DMAD in the reaction mixture. This implies that the two reaction pathways are independent from each other. Pyrrole derivatives are often formed upon rearrangements of the primary products of addition of DMAD to nitrones; in many cases, rearrangement starts with contraction of the isoxazole ring to give aziridine derivatives.[23] Aziridines including 1,3-diazabicyclo[3.1.0]hex-3-ene derivatives are able to react with dipolarophiles.[24] The reaction proceeds *via* opening of the aziridine ring to

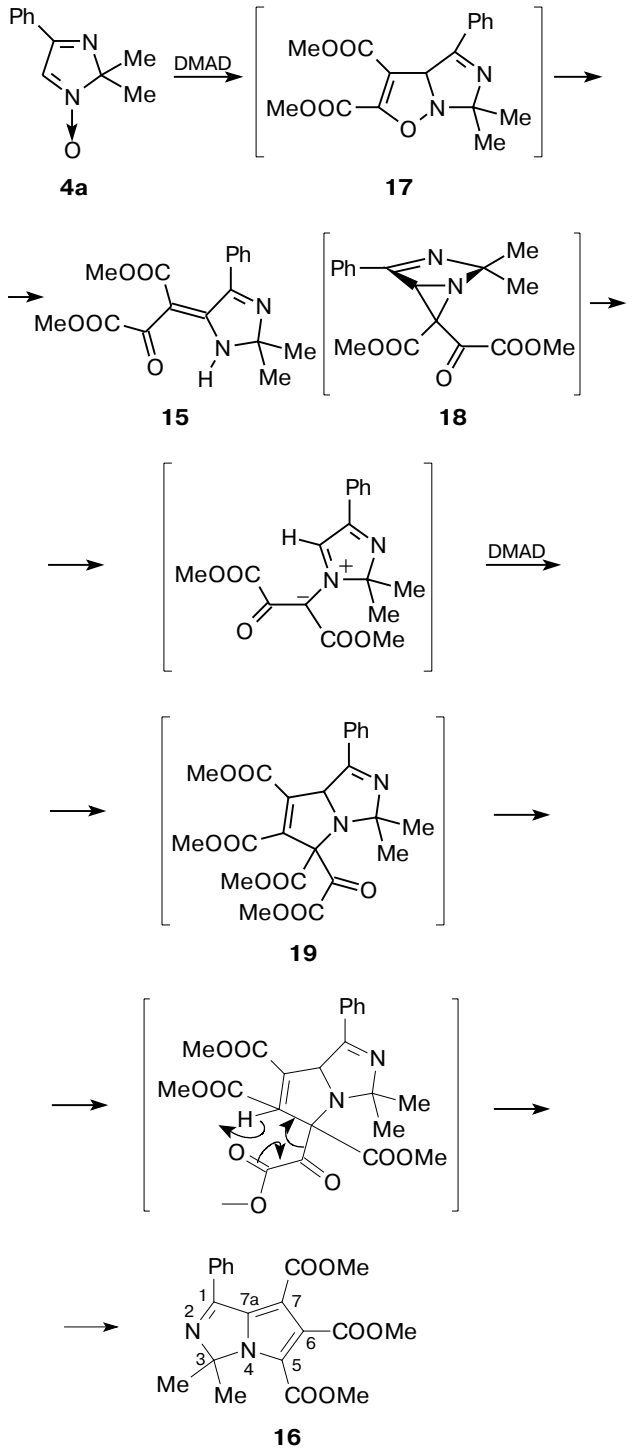
Table 5. NMR spectra of compounds **8**—**16**

Compound	Solvent	^{1}H NMR, δ, *J*/Hz	^{13}C NMR, δ
8	$CDCl_3$	1.49, 1.57 (both s, each 3 H, Me_{gem}); 3.20 (OMe); 3.92, 5.35 (both d, each 1 H, 2 CH, J = 8); 7.30, 7.45, 8.34 (all m; 2 H, 6 H and 2 H, 2 Ph)	22.8, 29.2 (Me_{gem}); 52.1 (OMe); 56.9, 83.4 (2 CH); 89.7 ($\underline{C}Me_2$); 163.5, 169.1 (C=O); 171.1 (Ph—C=N); Ph: 129.9 (C_i); 129.7 (C_o); 129.2 (C_m); 131.9 (C_p); N—Ph: 131.3 (C_i); 126.4 (C_o); 128.1 (C_m); 128.9 (C_p)
9	$(CD_3)_2SO$	1.47, 1.59 (both s, each 3 H, Me_{gem}); 3.26 (OMe); 4.04, 5.45 (both d, each 1 H, 2 CH, J = 8.5);7.25, 7.50 (m, 2 H and 3 H, N—Ph); 7.50, 7.96 (m, 3 H and 2 H, Ph)	19.4, 27.0 (Me_{gem}); 50.7 (OMe); 56.5, 82.4 (2 CH); 73.5 ($\underline{C}Me_2$); 120.2 (N—C—OMe); 169.6, 177.5 (C=O); 178.1 (Ph—C=N); Ph: 130.9 (C_i); 128.4 (C_o); 129.1 (C_m); 131.8 (C_p); N—Ph: 131.9 (C_i); 126.7 (C_o); 128.8 (C_m); 128.6 (C_p)
10	$CDCl_3$	1.40, 1.70 (both s, each 3 H, Me_{gem}); 4.28, 4.91 (both d, each 1 H, CH(3a), CH(8a), J = 8); 5.58 (s, 1 H, CH(3b)); 7.45, 7.78 (both m, 3 H and 2 H, Ph); 7.34—7.49 (m, 5 H, N—Ph);	20.9, 24.4 (Me_{gem}); 52.8, 74.9, 92.4 (3 CH); 78.3 ($\underline{C}Me_2$); 173.2, 177.5 (C=O); 173.7 (Ph—C=N); Ph: 131.3 (C_i); 128.5 (C_o); 129.1 (C_m); 130.8 (C_p); N—Ph: 131.8 (C_i); 128.2 (C_o); 129.1 (C_m); 128.6 (C_p)
11a	$(CD_3)_2SO$	1.30, 1.77 (both s, each 3 H, Me_{gem}); 4.02 (dd, 1 H, CH(3a), J_1 = 7.5, J_2 = 1.5); 4.82 (d, 1 H, CH(7a), J = 7.5); 5.12 (d, 1 H, CH(3b), J = 1.5); 7.50, 7.89 (both m, 3 H and 2 H, Ph); 7.30, 7.50 (both m, 2 H and 3 H, N—Ph)	22.3, 26.4 (Me_{gem}); 50.3, 75.1, 76.0 (3 CH); 96.5 ($\underline{C}Me_2$); 164.6, 173.8 (C=O); 173.6 (Ph—C=N); Ph: 130.7 (C_i); 128.1 (C_o); 129.1 (C_m); 131.2 (C_p); N—Ph: 131.1 (C_i); 126.1 (C_o); 129.0 (C_m); 128.9 (C_p)
11b	$(CD_3)_2CO$	1.19, 1.59 (both s, each 3 H, Me_{gem}); 4.02 (s, 3 H, OMe); 4.50 (dd, 1 H, CH(3a), J_1 = 7.5; J_2 = 1); 5.02 (d, 1 H, CH(7a), J = 7.5); 5.14 (d, 1 H, CH(3b), J = 1); 7.30, 7.50 (both m, 2 H and 3 H, N—Ph); 8.13 (s, 1 H, HC=N)	21.6, 25.2 (Me_{gem}); 62.6 (O—Me); 50.3, 75.0, 75.1 (3 CH); 95.7 ($\underline{C}Me_2$); 144.4 (HC=N); 160.6, 173.9 (C=O); 173.8 (Ph—C=N); N—Ph: 131.8 (C_i); 126.5 (C_o); 128.8 (C_m); 128.4 (C_p)
12	$(CD_3)_2CO$	1.45, 1.55 (both s, each 3 H, Me_{gem}); 3.37, 3.44, 3.86 (all s, each 3 H, 3 OMe); 7.45, 8.05 (m, 3 H and 2 H, N=C—Ph);	22.4, 30.4 (Me_{gem}); 50.6, 52.3, 53.7 (3 O—Me); 96.5 ($\underline{C}Me_2$); 163.1 (Ph—C=N); 108.0, 153.0 (C=C); 162.5, 158.5 (COOMe); Ph: 140.5 (C_i); 128.8 (C_o); 129.8 (C_m); 132.0 (C_p)
13	$(CD_3)_2CO$	1.59, 1.64 (both s, each 3 H, Me_{gem}); 3.35, 3.75, 3.89 (all s, each 3 H, 3 OMe); 7.53, 7.98 (both m; 3 H and 2 H, N=C—Ph)	20.9, 28.3 (Me_{gem}); 50.9, 52.2, 53.7 (3 O—Me); 77.9 ($\underline{C}Me_2$); 125.6 (N—C—OMe); 179.1 (Ph—C=N); 159.5, 162.0 (COOMe); 109.0, 156.5 (C=C); Ph: 132.1 (C_i); 129.5 (C_o); 129.5 (C_m); 132.2 (C_p)
14	$(CD_3)_2CO$	1.85 (s, 6 H, Me_{gem}); 3.71, 3.77 (both s, each 3 H, 2 OMe); 7.62, 8.23 (both m; 3 H and 2 H, Ph)	
14a	$(CD_3)_2CO$	0.81, 1.58 (both s, each 3 H, Me_{gem}); 3.65, 3.75 (both s, each 3 H, 2 OMe); 7.42, 7.60 (both m, 3 H and 2 H, Ph); 5.86 (br, 1 H, NH); 9.44, 9.09 (both br, 1 H, NH and OH)	20.3, 27.1 (Me_{gem}); 51.1, 51.7 (2 O—Me); 65.9 ($\underline{C}Me_2$); 163.4 ($(HN)_2C$=); 84.4 (C=C); 93.8 (HO—C—NH); 167.6, 168.3 (2 COOMe); 184.9 (C(O)COOMe) Ph: 140.1 (C_i); 127.2 (C_o); 129.1 (C_m); 129.5 (C_p)
15	$CDCl_3$	1.65 (s, 6 H, Me_{gem}); 2.82, 3.83 (both s, each 3 H, 2 OMe); 7.42 (s, 5 H, N=C—Ph)	24.6 (Me_{gem}); 49.5, 51.2 (2 O—Me); 93.0 ($\underline{C}Me_2$); 165.1 (Ph—C=N); 183.6 (C(2)); 93.3 (C=C); 157.4, 166.3 (2 COOMe); 134.6 (=C(OH)COOMe) Ph: 122.7 (C_i); 126.4 (C_o); 128.3 (C_m); 129.4 (C_p)
16*	$(CD_3)_2CO$	1.90 (s, 6 H, Me_{gem}); 3.42, 3.84, 3.88 (all s, each 3 H, 3 OMe); 7.57, 7.78 (m, 3 H and 2 H, N=C—Ph)	24.5 (Me_{gem}); 51.4 (O—Me); 52.6 (2 O—Me); 93.1 ($\underline{C}Me_2$); 162.7 (Ph—C=N); 107.2 (C(7)); 121.5 (C(6)); 131.4 (C(7a)); 139.2 (C(5)); 160.1, 160.3, 165.0 (3 COOMe); Ph: 133.7 (C_i); 128.5 (C_o); 129.5 (C_m); 131.0 (C_p)

* Mass spectrum, m/z ($I_{отн}$ (%)): 384 $[M]^+$ (100), 369 $[M - Me]^+$ (7), 353 $[M - OMe]^+$ (40).

give 1,3-dipole. Compound **16** is formed, apparently, according to Scheme 4. The cycloadduct **17** produced initially is either opened to give enamino ketone **15** or isomerizes to yield 1,3-diazabicyclo[3.1.0]hex-3-ene (**18**), which reacts with a second DMAD molecule to give cycloadduct **19**; this product undergoes a 1,3-sigmatropic shift and aromatization to give compound **16**.

Scheme 4



Thus, 2*H*-imidazole 1-oxide and 4*H*-imidazole 3-oxide derivatives can undergo 1,3-dipolar cycloaddition to dipolarophiles containing C—C and C=N multiple bonds. Depending on the dipolarophile structure, these reactions of α-methoxynitrones proceed either more rapidly or more slowly than the reactions of the corresponding aldonitrones.

Experimental

IR spectra were recorded on Specord M-80 and Bruker IFS 66 spectrometers in KBr pellets (concentration 0.25%, pellet thickness 1 mm). UV spectra were recorded on a Specord UV-VIS instrument in EtOH solutions. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer for 1—5% solutions using the solvent signal as the standard. The ^{13}C NMR signals were assigned based on the analysis of intensities of spectra with *J*-modulation and published data.[4,10,25—27] Mass spectra were run on a Finnigan MAT 8200 mass spectrometer under direct injection conditions (EI, 70 eV). Nitrones **1**—**4a**,**b** were prepared by procedures published previously.[4,5,10] All solvents were purified by distillation; CH_2Cl_2 was additionally distilled over P_2O_5.

6,6-Dimethyl-3a-methoxy-4-phenyl-3a,6a-dihydro-3*H*-imidazo[1,5-*b*][1,2,4]oxadiazol-2-one (5a—d), 6,6-dimethyl-5-phenyl-3a,6-dihydro-3*H*-imidazo[1,2-*b*][1,2,4]oxadiazol-2-ones (6a—d, 7a—d) (general procedure). Isocyanate or isothiocyanate (2 mmol) was added to a solution of nitrones **1**, **2**, or **3** (2 mmol)[10] in 10 mL of CH_2Cl_2. The reaction mixture was allowed to stand at 25 °C until the initial nitrone disappeared (TLC, Silufol UV-254, $CHCl_3$—MeOH, 50 : 1, as the eluent), applied onto a column with silica gel Kieselgel 60 (Merck), and eluted with $CHCl_3$. The reaction times and the product yields, physicochemical properties, and spectra are presented in Tables 1—4. The resulting compounds were recrystallized from a 1 : 1 hexane—Et_2O mixture.

5,5-Dimethyl-2,7-diphenyl-3a,4a,7a,7b-tetrahydro-4-oxa-2,4a,5,-triazacyclopenta[*a*]pentalene-1,3-dione (8, 11a,b), 5,5-dimethyl-2,6-diphenyl-3a,4a,7a,7b-tetrahydro-4-oxa-2,4a,7-triazacyclopenta[*a*]pentalene-1,3-diones (9, 10). Nitrones **1**—**4a**,**b** (2 mmol) and *N*-phenylmaleimide (2 mmol, Lancaster) were dissolved in 1 mL of $CHCl_2$. After 24 h, the precipitated compounds **8**, **10**, and **11a**,**b** were filtered off and recrystallized from MeOH. The solution of nitrone **2** and *N*-phenylmaleimide was kept for 10 days, the reaction mixture was diluted with 5 mL of cooled MeOH, and the precipitate was filtered off and recrystallized from MeOH to give product **9** (see Table 2 and 5).

Dimethyl 6,6-dimethyl-3a-methoxy-4-phenyl-3a,6-dihydroimidazo[1,5-*b*]isoxazole-2,3-dicarboxylate (12) and dimethyl 3a-methoxy-6,6-dimethyl-5-phenyl-3a,6-dihydroimidazo[1,2-*b*]isoxazole-2,3-dicarboxylate (13). DMAD (Merck) (3 mmol) was added to a solution of methoxynitrone **1** and **2** (2 mmol) in 10 mL of CH_2Cl_2; after 24 h, the reaction mixture was applied onto a column with silica gel Kieselgel 60 (Merck) and eluted with $CHCl_3$. The products **12** and **13** were recrystallized from hexane (see Table 2 and 5).

Dimethyl 2-(5,5-dimethyl-4-phenyl-2,5-dihydro-1*H*-imidazol-2-ydene)-3-oxosuccinate (14) was prepared similarly to ester **12** from nitrone **3**. **Dimethyl 2-(2,2-dimethyl-4-phenyl-2,5-dihydro-1*H*-imidazol-5-ylidene)-3-oxosuccinate (15), trimethyl 3,3-dimethyl-1-phenyl-3*H*-pyrrolo[1,2-*c*]imidazole-5,6,7-tricarboxylate (16)** were prepared similarly to **12** from aldonitrone **4a**; complete conversion of the reactant was attained by using a twofold excess of DMAD. Compounds **14**, **15**, and **18** were recrystallized from a 1 : 1 hexane—AcOEt mixture.

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References

1. K. B. G. Torsell, in *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis. Novel Strategies in Synthesis*, VCH Publ., Inc., Weinheim, 1988, 75.
2. J. J. Tufariello, *Acc. Chem. Res.*, 1979, **12**, 396.
3. E. Breuer, in *Nitrones, Nitronates and Nitroxides*, Eds. S. Patai and Z. Rappoport, J. Wiley and Sons, Chichester, 1989, 245.
4. I. A. Grigor´ev, I. A. Kirilyuk, and L. B. Volodarskii, *Khim. Geterotsikl. Soedinenii*, 1988, 1640 [*Chem. Heterocycl. Compd.*, 1988 (Engl. Transl.)].
5. I. A. Kirilyuk, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2113 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 1871 (Engl. Transl.)].
6. I. A. Kirilyuk, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2122 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 1880 (Engl. Transl.)].
7. I. A. Kirilyuk, I. A. Grigor´ev, O. P. Petrenko, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 2096 [*Russ. Chem. Bull.*, 1993, **42**, 2010 (Engl. Transl.)].
8. I. A. Grigor´ev, I. A. Kirilyuk, and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 1624 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 1488 (Engl. Transl.)].
9. I. V. Nechepurenko, O. P. Petrenko, I. A. Grigor´ev, and L. B. Volodarskii, *Zh. Org. Khim.*, 1997, **33**, 767 [*Russ. J. Org. Chem.*, 1997, **33** (Engl. Transl.)].
10. S. M. Bakunova, I. A. Grigor´ev, I. A. Kirilyuk, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.,* 1999, 2160 [*Russ. Chem. Bull.,* 1999, **49**, 2136 (Engl. Transl.)].
11. B. A. J. Clark, T. J. Evans, and R. G. Simmonds, *J. Chem. Soc., Perkin Trans. 1,* 1975, 1803.
12. J. B. Hendrickson and D. A. Pearson, *Tetrahedron Lett.,* 1983, **24**, 4657.
13. S. P. Ashburn and R. M. Coates, *J. Org. Chem.,* 1985, **50**, 3076.
14. S. P. Ashburn and R. M. Coates, *J. Org. Chem.,* 1984, **49**, 3127.
15. T. Hisano, K. Harano, T. Matsuoka, S. Watanabe, and T. Matsuzaki, *Chem. Pharm. Bull.,* 1989, **37**, 907.
16. J. J. Tufariello, in *The Chemistry of 1,3-dipolar Cycloaddition*, Ed. A. Padwa, Willey Interscience, New York, 1984, **2**, 101.
17. I. G. Kursakina, V. F. Starichenko, I. A. Kirilyuk, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.*, 1991, 2009 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.,* 1991, **40**, 1774 (Engl. Transl.)].
18. I. G. Irtegova, I. A. Grigor´ev, I. A. Kirilyuk, and V. F. Starichenko, *6th Intern. Symp. on Spin Trapping. Spin Traps, Nitroxides and Nitric Oxide. Prog. and Abstr., (Marseilles, August 27—31, 2000)*, Université d´Aix-Marseille 3, Université de Provence, CNRS, Marseilles, 2000, 64.
19. D. St. C. Black and K. G. Watson, *Austr. J. Chem.,* 1973, **26**, 2473.
20. M. A. Voinov, V. V. Martin, and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1992, 2642 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.,* 1992, **41**, 2091 (Engl. Transl.)].
21. M. Mosui, K. Suda, M. Jamauchi, and C. Yizima, *Chem. Pharm. Bull.*, 1973, **21**, 1605.
22. L. B. Volodarskii, L. A. Fust, and V. S. Kobrin, *Khim. Geterotsikl. Soedinenii*, 1972, 1246 [*Chem. Heterocycl. Compd.,* 1972 (Engl. Transl.)].
23. J. P. Freeman, *Chem. Rev.,* 1983, **83**, 241.
24. H. W. Heine, A. B. Smith, and J. D. Bower, *J. Org. Chem.*, 1968, **33**, 1097.
25. I. A. Grigor´ev, V. V. Martin, G. I. Shchukin, V. I. Mamatyuk, and L. B. Volodarskii, *Khim. Geterotsikl. Soedinenii*, 1985, 247 [*Chem. Heterocycl. Compd.,* 1985 (Engl. Transl.)].
26. I. A. Grigor´ev, G. I. Shchukin, V. V. Martin, and V. I. Mamatyuk, *Khim. Geterotsikl. Soedinenii*, 1985, 252 [*Chem. Heterocycl. Compd.,* 1985 (Engl. Transl.)].
27. I. A. Grigor´ev, V. I. Mamatyuk, G. I. Shchukin, V. V. Martin, and L. B. Volodarskii, *Khimiya Geterotsikl. Soedinenii*, 1986, 1065 [*Chem. Heterocycl. Compd.,* 1986 (Engl. Transl.)].

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