

SYNTHESIS OF ISOXAZOLES BEARING METHOXYCARBONYL AND FORMYL GROUPS BY 1,3-DIPOLAR CYCLOADDITION OF NITRILE OXIDES TO OLEFINIC AND ACETYLENIC DIPOLAROPHILES

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Abstract- The 1,3-dipolar cycloadditions of benzo-, bromoformo- and acetonitrile oxides to enamino ester (1) and acetylenic esters (2, 3) afforded functionalized isoxazoles in moderate to good yields. Cycloadditions with the enamino ester (1) gave the corresponding methyl 5-dimethoxymethylisoxazole-4-carboxylate (7a-9a) as the sole regioisomer, whereas the reactions with acetylenic dipolarophiles (2, 3) were generally less selective and the regioselectivity depended significantly on the nature of the substituents of the dipole and the acetylenic ester.

INTRODUCTION

Isoxazoles display interesting biological activities¹ and have been used as key intermediates in natural product synthesis² and for preparing several pharmacological active compounds.³ The 1,3-dipolar cycloaddition of nitrile oxides to alkenes has been one of the most general methods for the construction of isoxazolines.^{3a,4}

In a recent paper⁵ we have reported the cycloaddition of nitrile oxides to 4-oxobut-2-enoic acid derivatives that afford functionalized isoxazolines. In order to obtain the corresponding isoxazoles a separate dehydrogenation reaction of the isoxazolines would be necessary. In the present paper we have studied direct routes to these functionalized isoxazoles by using the enamino ester (1) and the acetylenic derivatives (2 and 3) as dipolarophiles. According to literature,^{3a,4,6} cycloadditions of nitrile oxides to enamino esters occurred with elimination of the amine to give regiospecifically the isoxazole-4-carboxylate. Moreover alkynes, although displayed lower dipolarophilic activity than alkenes, also afforded the isoxazoles in a single operation. However, there are few reports dealing with the use of 4-oxobut-2-ynoic acid derivatives as dipolarophiles, the only examples being the cycloaddition of diazo compounds,⁷⁻⁹ sydnone^{8,9} and azides^{8,9} described by us.

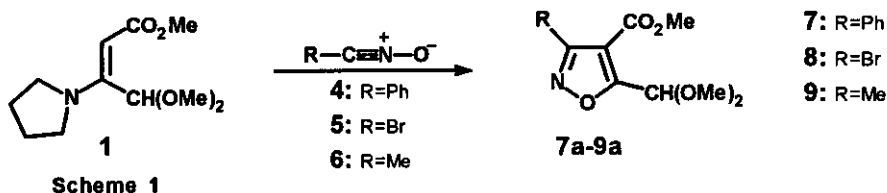
RESULTS AND DISCUSSION

Benzonitrile oxide (BNO) (4) and bromoformonitrile oxide (5) were prepared by dehydrohalogenation of the corresponding hydroximic acid halides. The cycloadditions to acetylenic esters (2 and 3) were conducted at room temperature with the equimolecular amount or in excess of dipolarophile, whereas an excess of dipole was used in the reactions with enamine (1). The acetonitrile oxide (6) was generated "in situ" from nitroethane by the Mukaiyama's method.¹⁰

Cycloadditions to methyl 4,4-dimethoxy-3-(pyrrolidin-1-yl)but-2-enoate

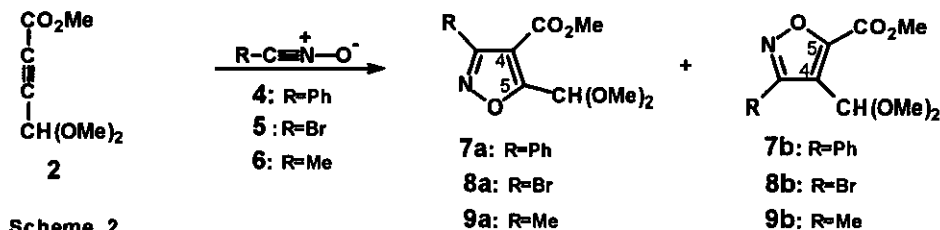
Nitrile oxides (4-6) reacted smoothly with enamine (1) to afford, with concomitant elimination of pyrrolidine, the expected 4-methoxycarbonylisoxazoles (7a-9a) in moderate yields. As summarized in Table I, only one detectable adduct was formed in each case.

The regioselectivity observed in these cycloadditions is in accord with the behavior of other β -amino- α,β -unsaturated esters^{3a,4,6} towards this type of dipole. On the basis of the reported observations we have assigned the structures (7a-9a) to the isolated isoxazol derivatives (Scheme 1).



Cycloadditions to methyl but-2-ynoates

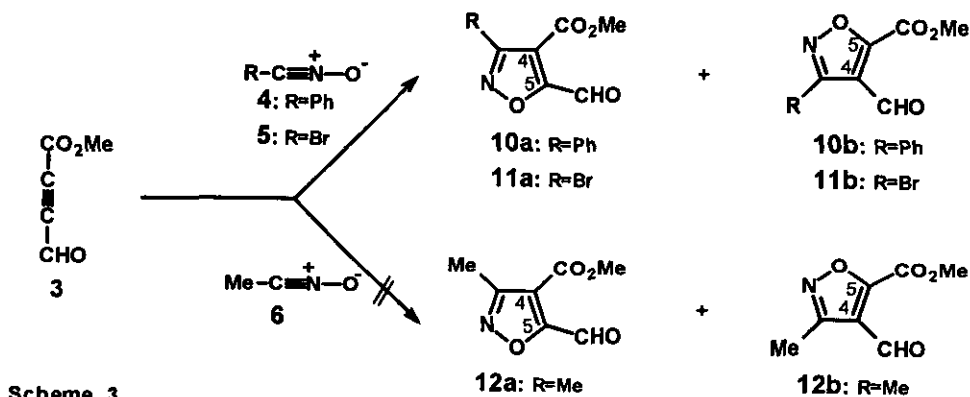
Cycloaddition of nitrile oxides (4-6) to methyl 4,4-dimethoxybut-2-ynoate (2) proceeded readily affording high yields of the isoxazoles (7-9) respectively, as mixtures of regioisomers. The results obtained and the experimental conditions employed are summarized in Table I. The predominant orientation in the addition of the nitrile oxides (4-6) to the acetal ester (2) is the same as that observed in the cycloaddition with enamine (1).



However, the regioselectivity with the acetylenic acetal (2) is lower and depends also significantly on the nature of the substituent R of the dipole ($a/b = 9.0$, 1.5, and 2.3 for benzo-, bromoformo-, and acetonitrile oxides, respectively). These results are noteworthy since the behavior of nitrile oxides (5 and 6) towards acetylenic esters has been scarcely studied^{11,12} and the a/b ratios obtained differ basically from those observed by us in cycloadditions to methyl 4,4-dimethoxybut-2-enoates.⁵

The structure of the isoxazoles (7b-9b) was established by comparison of their ¹H-nmr spectra with those of the regioisomeric isoxazoles (7a-9a). As can be observed in Table II, the acetalic proton of the 4-methoxycarbonylisoxazoles (major regioisomer) appears at higher chemical shift (δ) than that for the regioisomers (7b-9b). According to this assignment, the methoxycarbonyl group in regioisomers of type a resonates at lower δ value than that of the corresponding b isomers.^{6a}

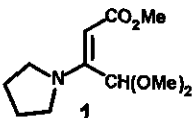
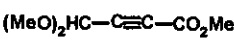
The ester aldehyde (3) is a very active dipolarophile and reacts readily with dipoles (4 and 5) to give mixtures of the regioisomeric isoxazoles in good yields. However with acetonitrile oxide (6), because of competing side reactions, we could not detect the formation of isoxazoles (12) in the crude reaction mixture. Moreover, the desired formylisoxazoles (12a and 12b) were obtained in good yields by formolysis of the corresponding acetals (9a and 9b), respectively.



The assignments of the regioisomeric structures a or b to formylisoxazoles (10) were made by comparison of their ¹H-nmr spectra with those of the isoxazoles (10a and 10b) obtained by hydrolysis of their acetals (7a and 7b), respectively. Structural assignments of the bromo(formyl)isoxazoles (11a and 11b) were made by conversion into the corresponding acetals. As can be observed in Table II, the chemical shift of the aldehydic proton of the 5-methoxycarbonylisoxazoles (10b-12b) is higher than that in their regioisomers (10a-12a). This observation is in contrast to the behaviour of the corresponding acetalic protons mentioned above.

It is noteworthy that in the cycloaddition of BNO to aldehyde (3) the predominant orientation is the same as

Table I. Cycloadditions to methyl (*E*)-4,4-dimethoxy-3-(1-pyrrolidinyl)but-2-enoate, 4,4-dimethoxy-, and 4-oxobut-2-ynoates

Dipolarophile	Dipole R	N ^o	Ester/dipole	°C (h)	Products	Ratio a/b	Yield %
 1	Ph	(4)	0.5	20 (72)	7a	100:0	52
	Br	(5)	1	20 (3)	8a	100:0	60
	Me	(6)	0.7	60 (4)	9a	100:0	55
 2	Ph	(4)	3.3	20 (24)	7a+7b	90:10	90
	Ph	(4)	3.3	110 (24) ^a	7a+7b	90:10	90
	Br	(5)	1.5	20 (4)	8a+8b	60:40	90
	Me	(6)	1.0	20 (5)	9a+9b	70:30	70
 3	Ph	(4)	3.3	20 (1)	10a+10b	65:35	85
	Ph	(4)	3.3	110 (5) ^a	10a+10b	65:35	75
	Br	(5)	1.5	20 (2)	11a+11b	15:85	90
	Me	(6)	1.0	20 (2)	- ^b		

^aIn absence of base. ^bCycloadduct was not detected.**Table II.** ¹H-Nmr data of isoxazoles (7-12)

Comp.	R	CH(OMe) ₂	CHO	CO ₂ Me	(OMe)	R
7a	Ph	6.00	-	3.79	3.50	7.70-7.50, 7.50-7.35
7b	Ph	5.95	-	3.98	3.38	8.05-7.88, 7.50-7.31
10a	Ph	-	10.32	3.87	-	7.90-7.60, 7.55-7.35
10b	Ph	-	10.53	4.08	-	7.93-7.65, 7.60-7.33
8a	Br	5.97	-	3.90	3.40	-
8b	Br	5.80	-	3.97	3.38	-
11a	Br	-	10.27	4.00	-	-
11b	Br	-	10.40	4.07	-	-
9a	Me	6.00	-	3.90	3.47	2.46
9b	Me	5.80	-	3.97	3.48	2.40
12a	Me	-	10.30	3.94	-	2.51
12b	Me	-	10.45	4.03	-	2.54

for acetal (2), in contrast to the regiochemistry observed for additions of diazoalkanes, sydnone, azides and other nitrile oxides to dipolarophiles (2 and 3).

The higher reactivity of aldehyde (3) and the differences observed in the regiochemistry compared to 2 can be ascribed to the presence of a second strongly electron-withdrawing group attached to the alkyne.⁴

In summary, the results described herein indicate that nitrile oxides (4-6) add regiospecifically to enamino ester (1). A decrease in regiocontrol is observed in the cycloadditions with the acetylenic ester acetal (2), especially with bromoformo- and acetonitrile oxides, although in all cases the major adduct is the isoxazole-4-carboxylate as in the reactions of enamine (1). In contrast, cycloaddition of the ester aldehyde (3) to the 1,3-dipole (5) proceeds with the opposite regiochemistry. The above reactions provide a convenient entry to functionalized isoxazoles that are valuable intermediates, in particular for the synthesis of fused heterocyclic ring systems.

EXPERIMENTAL

Mps are uncorrected. Microanalyses were performed with a Heraeus analyzer. Ir spectra were recorded on a Perkin-Elmer model 681 spectrophotometer ($\nu_{\max}$, cm^{-1}). ^1H - and ^{13}C -nmr spectra were obtained on a Varian EM-390 or a Bruker WP 200SY spectrometer for CDCl_3 solutions, using TMS ($\delta=0$ ppm) as internal reference. Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 230-400 mesh and DC-Alufolien 60 were used for flash and analytical thin layer chromatography, respectively.

The dipolarophiles (1,¹³ 2¹⁴ and 3⁹) were prepared according to the previously reported procedures.

Cycloaddition of Nitrile Oxides (4-6) to Methyl (E)-4,4-Dimethoxy-3-(pyrrolidin-1-yl)but-2-enoate

Methyl 5-Dimethoxymethyl-3-phenylisoxazole-4-carboxylate (7a)

To an ice cooled solution of methyl (E)-4,4-dimethoxy-3-(pyrrolidin-1-yl)but-2-enoate (1) (916 mg, 4 mmol) in methylene chloride (25 ml) was added with stirring triethylamine (1.24 ml, 9 mmol). To the stirred solution was added benzaldehyde chloroxime (622 mg, 4 mmol) in small portions. After 1 day at room temperature, a new portion of benzaldehyde chloroxime (622 mg, 4 mmol) was added and the mixture allowed to stand for 2 days. The solvent was removed under reduced pressure and, after addition of hexane, the precipitate was filtered off and the solution washed several times with water. The organic layer was dried (MgSO_4), and after removing of solvent the crude residue analyzed by ^1H -nmr contained only the isoxazole (7a) and dimers of benzonitrile oxide. The products were separated by column chromatography (hexane-ethyl acetate, 3:2). Total yield 52% (576 mg). Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_5$: C, 60.65; H, 5.41; N, 5.05. Found: C, 60.30; H, 5.42; N, 5.13. Ir (film): 1735, 1630, 1610, 1580. ^{13}C -Nmr: 171.4 (C-5), 161.8 (C=O), 161.6 (C-3), 129.9 (Ar), 129.0 (Ar), 128.1 (Ar), 127.6 (Ar), 109.6 (C-4), 96.2 (C_{AcH}), 54.2 (OMe), 52.0 (OMe). Ms, m/z (%): 277 (2), 262 (16), 246 (14), 218 (10), 202 (13), 75 (100).

Methyl 3-Bromo-5-dimethoxymethylisoxazole-4-carboxylate (8a)

To a vigorously stirred mixture of methyl (E)-4,4-dimethoxy-3-(pyrrolidin-1-yl)but-2-enoate (1) (687 mg, 3 mmol), ethyl acetate (15 ml), potassium bicarbonate (660 mg, 6.6 mmol), and water (1 ml), was added solid dibromoformaldoxime (670 mg, 3.3 mmol) in small portions. Stirring was maintained during 3 h at room temperature. The precipitated salts were filtered off, the filtrate was dried (MgSO_4) and the solvent removed under reduced pressure. In the residue only the isoxazole (8a) was detected by ^1H -nmr. The crude product was chromatographed on silica gel (ethyl acetate-hexane 1:1) to afford the pure isoxazole (8a) in 60 % yield (504 mg). Recrystallized from petroleum ether mp 58-60 °C. Anal. Calcd for $\text{C}_8\text{H}_{10}\text{NO}_5\text{Br}$: C, 34.28; H, 3.57; N, 5.15.

5.00; Br, 28.57. Found: C, 34.60; H, 3.66; N, 5.30; Br, 28.32. Ir (nujol): 1730, 1610. ^{13}C -Nmr: 172.8 (C-5), 159.9 (C=O), 140.4 (C-3), 109.4 (C-4), 95.8 (C_{Ac}), 54.5 (OMe), 52.4 (OMe). Ms, m/z (%): 282-280 (1), 250-248 (70), 200 (11), 168 (58), 139 (62), 75 (100).

Methyl 5-Dimethoxymethyl-3-methylisoxazole-4-carboxylate (9a)

To a stirred solution of methyl (*E*)-4,4-dimethoxy-4-(pyrrolidin-1-yl)but-2-enoate (**1**) (458 mg, 2 mmol) and triethylamine (1 ml) in toluene (6 ml) was added dropwise a solution of nitroethane (225 mg, 3 mmol) in toluene (3 ml), and phenyl isocyanate (595 mg, 5 mmol). The reaction mixture was heated at 60 °C for 4 h, then cooled to room temperature. The precipitated *N,N*-diphenylurea was filtered off and the solvent was removed to give a residue, that was purified by column chromatography (ethyl acetate-hexane 1:1). Yield 55 % (236 mg). Anal. Calcd for $\text{C}_9\text{H}_{13}\text{NO}_5$: C, 50.23; H, 6.04; N, 6.51. Found: C, 50.06; H, 6.28; N, 6.70. Ir (film): 1730, 1620. ^{13}C -Nmr: 171.3 (C-5), 161.7 (C=O), 159.3 (C-3), 109.6 (C-4), 96.0 (C_{Ac}), 54.2 (OMe), 51.7 (OMe), 11.3 (Me). Ms, m/z (%): 200 (18), 184 (76), 168 (23), 97 (12), 75 (100), 69 (11).

Cycloaddition of Benzonitrile Oxide (4) to Methyl But-2-ynoates (2 and 3)

a) To an ice cooled solution of methyl 4,4-dimethoxybut-2-ynoate (**2**) (316 mg, 2 mmol) and benzaldehyde chloroxime (100 mg, 0.6 mmol) in ether (10 ml) was added with stirring triethylamine (60 mg, 0.6 mmol) in ether (3 ml). The mixture was allowed to stand at room temperature for 24 h, the precipitated salt was filtered off and washed with ether. The combined organic layers were washed several times with water, the organic layer was dried (MgSO_4) and, after removing the solvent, afforded an oil that analyzed by ^1H -nmr contained the isoxazoles (**7a** and **7b**) (90:10), which were purified by column chromatography (petroleum ether-ethyl acetate 9:1). Yield 90 % (149 mg).

Methyl 4-Dimethoxymethyl-3-phenylisoxazole-5-carboxylate (7b)

Ir (film): 1740, 1610, 1580. Ms, m/z (%) : 277 (2), 262 (12), 246 (18), 230 (8), 218 (6), 202 (28), 143 (14), 115 (18), 77 (75), 75 (100), 59 (24).

b) A solution of **2** (316 mg, 2 mmol) and benzaldehyde chloroxime (100 mg, 0.6 mmol) in toluene (10 ml) was heated under reflux during 24 h. The solvent was removed in vacuo and the residue purified by the procedure outlined above. Yield 90 % (149 mg).

c) Following the procedure a) outlined above, methyl 4-oxobut-2-ynoate (**3**) (224 mg, 2 mmol), after 1 h afford the isoxazoles (**10a** and **10b**) in a 65:35 ratio, determined by ^1H -nmr. The products were separated by column chromatography (petroleum ether-ethyl acetate 8:2). Total yield 85% (118 mg).

d) Following the procedure b) from methyl 4-oxobut-2-ynoate (**3**) (224 mg, 0.2 mmol), after 5 h, was obtained a mixture of isoxazoles (**10a** and **10b**) in a 65:35 ratio. Total yield 75% (104 mg).

Methyl 5-Formyl-3-phenylisoxazole-4-carboxylate (10a)

Anal. Calcd for $\text{C}_{12}\text{H}_9\text{NO}_4$: C, 62.33; H, 3.89; N, 6.66. Found: C, 62.10; H, 4.27; N, 6.22. Ir (film): 1740, 1710, 1635, 1600. Ms, m/z : 231 (29), 202 (13), 172 (33), 143 (56), 104 (42), 77 (100), 59 (33).

Methyl 4-Formyl-3-phenylisoxazole-5-carboxylate (10b)

Anal. Calcd for $\text{C}_{12}\text{H}_9\text{NO}_4$: C, 62.33; H, 3.89; N, 6.66. Found: C, 62.48; H, 4.10; N, 6.46. Ir (film): 1740, 1700, 1630, 1610. Ms, m/z : 231 (25), 202 (12), 175 (33), 172 (29), 144 (36), 104 (100), 77 (75), 59 (20).

Cycloaddition of Bromoformonitrile Oxide (5) to Methyl But-2-ynoates (2 and 3)

a) To a vigorously stirred mixture of methyl 4,4-dimethoxybut-2-ynoate (**2**) (474 mg, 3 mmol), ethyl acetate (15 ml), potassium bicarbonate (400 mg, 4 mmol), and water (1 ml), was added solid dibromoformaldoxime (406 mg, 2 mmol) in small portions. After 4 h at room temperature the precipitate was filtered off, the solution was dried (MgSO_4) and the solvent removed. $^1\text{H-Nmr}$ analysis showed the presence of **8a** and **8b** in a 60:40 ratio. Attempts to separate the isoxazoles (**8a** and **8b**) by column chromatography on silica gel were unsuccessful. Total yield 90% (756 mg).

The above mixture was treated with 3 ml of 99-100% formic acid and then was allowed to stand at room temperature for 48 h. The formic acid and the ethyl formate were removed under reduced pressure and the isoxazoles (**11a** and **11b**) were isolated by column chromatography (petroleum ether-ethyl acetate 8:2).

Methyl 3-Bromo-5-formylisoxazole-4-carboxylate (11a)

Recrystallized from cyclohexane mp 61-63 °C. Anal. Calcd for $\text{C}_6\text{H}_4\text{NO}_4\text{Br}$: C, 30.77; H, 1.71; N, 5.98; Br, 34.19. Found: C, 31.05; H, 2.00; N, 5.68; Br, 33.97. Ir (nujol): 1740, 1700, 1600. Ms, m/z: 236-234 (10), 204-202 (12), 176-174 (6), 126 (43), 59 (100).

Methyl 3-Bromo-4-formylisoxazole-5-carboxylate (11b)

Recrystallized from cyclohexane mp 68-70 °C. Anal. Calcd for $\text{C}_6\text{H}_4\text{NO}_4\text{Br}$: C, 30.77; H, 1.71; N, 5.98; Br, 34.19. Found: C, 30.99; H, 2.01; N, 5.77; Br, 34.35. Ir (nujol): 1750, 1705, 1605. Ms, m/z: 236-234 (18), 204-202 (18), 176-174 (9), 126 (49), 94 (45), 59 (100).

The isoxazoles (**8a** and **8b**) were obtained, in quantitative yield, by acetalization of the corresponding aldehyde ester (**11a** and **11b**) with methyl orthoformate, in presence of methanol and *p*-toluenesulfonic acid.

Methyl 3-Bromo-4-dimethoxymethylisoxazole-5-carboxylate (8b)

Recrystallized from petroleum ether mp 72-73 °C. Anal. Calcd for $\text{C}_8\text{H}_{10}\text{NO}_3\text{Br}$: C, 34.28; H, 3.57; N, 5.00; Br, 28.57. Found: C, 34.40; H, 3.56; N, 5.20; Br, 28.33. Ir (nujol): 1740, 1610. Ms, m/z: 280-278 (1), 250-248 (57), 234-232 (12), 222-220 (11), 110 (100), 75 (50), 59 (66).

b) Starting from methyl 4-oxobut-2-enoate (**3**) (3 mmol) and dibromoformaldoxime (2 mmol), following the above procedure, after 2 h at room temperature was obtained a mixture which contained the regioisomeric isoxazoles (**11a** and **11b**) in a 15:85 ratio. The isoxazoles were isolated by column chromatography (petroleum ether-ethyl acetate 8:2). Total yield 90% (632 mg).

Cycloaddition of Acetonitrile Oxide (6) to Methyl But-2-ynoates (1 and 2)

a) To a stirred solution of methyl 4,4-dimethoxybut-2-ynoate (**2**) (474 mg, 3 mmol) and phenyl isocyanate (535 mg, 5 mmol) in anhydrous benzene (10 ml), at 0 °C, was added dropwise a solution of nitroethane (225 mg, 3 mmol) and two drops of triethylamine in benzene (3 ml). Stirring was maintained during 5 h at room temperature. The precipitated *N,N*-diphenylurea was filtered off. Evaporation of solvent gave a residue, whose $^1\text{H-nmr}$ analysis showed the presence of **7a** and **7b** in a 70:30 ratio. The products were separated by column chromatography (petroleum ether-ethyl acetate, 9:1). Total yield 70% (452 mg).

Methyl 4-Dimethoxymethyl-3-methylisoxazole-5-carboxylate (9b)

Anal. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.04; N, 6.51. Found: C, 50.14; H, 6.44; N, 6.64. Ir (film): 1740, 1610. Ms, m/z: 216 (5), 200 (8), 184 (87), 168 (11), 75 (100), 59 (6).

b) Following the procedure outlined above, the butynoate (3) after 2 h gave a complex mixture in which the regioisomeric isoxazoles (12a or 12b) could not be detected by 1H -nmr analysis. The same result was obtained when 2,6-dimethylpyridine or potassium carbonate was employed as a base.

Formolysis of Acetals 9a,b

To ester-acetal (9a) (215 mg, 1 mmol) was added formic acid (3 ml, of 99-100%) and the mixture was allowed to stand at room temperature for 12 h. After removing formic acid and methyl formate under reduced pressure was obtained 12a. Yield 95 % (161 mg). Identical result was obtained in the formolysis of 9b.

REFERENCES AND NOTES

1. a) P. Pevarello, R. Amici, M. Colombo, and M. Varasi, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2151. b) F. Lepage, F. Tombret, G. Cuvier, A. Marivain, and J. M. Gillardin, *Eur. J. Med. Chem.*, **1992**, 27, 581.
2. a) P. G. Baraldi, A. Barco, S. Benetti, G. P. Pollini, and D. Simoni, *Synthesis*, **1987**, 857. b) P. G. Baraldi, F. Moroder, G. P. Pollini, D. Simoni, A. Barco, and S. Benetti, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 2983. c) J. W. Patterson, P. S. Cheung, and M. J. Ernest, *J. Med. Chem.*, **1992**, 35, 507.
3. a) P. Grünanger and P. Vita-Finzi, in "The Chemistry of Heterocyclic Compounds", Vol. 49, ed. E. C. Taylor, J. Wiley & Sons, New York, 1991. b) S. Kanemasa and O. Tsuge, *Heterocycles*, **1990**, 30, 719.
- c) A. L. Smith, C. K. Hwang, E. Pitsinos, G. R. Scarlato, and K. C. Nicolaou, *J. Am. Chem. Soc.*, **1992**, 114, 3134. d) N. Sewald and K. Burger, *Ann. Chem.*, **1992**, 947.
4. "1,3-Dipolar Cycloaddition Chemistry", ed. Padwa A., Wiley-Interscience, New York, **1984**.
5. F. Fariña, M. R. Martín, M. V. Martín, and A. Martínez de Guereñu, *Heterocycles*, **1994**, 38, in press.
6. a) M. Christl, R. Huisgen, and R. Sustmann, *Chem. Ber.*, **1973**, 106, 3275. b) K. D. Bowles, D. Quincy, B. Mallet, J. I. McKenna, and N. R. Natale, *J. Chem. Educ.*, **1985**, 62, 1118. c) R. C. F. Jones, G. Bhalay, and P. A. Carter, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1715.
7. F. Fariña, M. V. Martín, and F. Sánchez, *An. Quím.*, **1982**, 78 C, 332.
8. F. Fariña, P. Fernández, M. R. Martín, M. V. Martín, and F. Sánchez, *An. Quím.*, **1983**, 75 C, 333.
9. F. Fariña, P. Fernández, M. T. Fraile, M. R. Martín, and M. V. Martín, *Heterocycles*, **1989**, 29, 967.
10. T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, **1960**, 82, 5339.
11. a) M. Christl and R. Huisgen, *Chem. Ber.*, **1973**, 106, 3345. b) M. Hojo, K. Tomita, and A. Hosomi, *Tetrahedron Lett.*, **1993**, 34, 485.
12. D. Chiarino, M. Napoletano, and A. Sala, *J. Heterocycl. Chem.*, **1987**, 24, 43.
13. B. de Ancos, F. Fariña, M. C. Maestro, and M. R. Martín, *Synthesis*, **1988**, 136.
14. F. Fariña, M. R. Martín, M. V. Martín, and F. Sánchez, *Synthesis*, **1977**, 641.

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