1,3-DIPOLAR CYCLOADDITIONS WITH METHYL 4-OXO- AND 4-HYDROXY-2-BUTYNOATES. SYNTHESIS OF FUNCTIONALIZED PYRAZOLES AND TRIAZOLES

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Abstract- The 1,3-dipolar cycloadditions of acetylenic esters **1-3** with diazo compounds, sydnones and p-methoxyphenyl azide proceed in good yields and afford functionalized pyrazoles and triazoles. Cycloadditions with the acetal **1** occur with high regioselectivity, whereas the reactions with the alcohol **3** are less selective. The aldehyde **2** is more reactive than **1** or **3** and cycloadditions proceed with lower regioselectivity, normally in opposite sense with respect to **1**.

The 1,3-dipolar cycloaddition with alkynic dipolarophiles represents a versatile method for the synthesis of a variety of five-membered heterocyclic compounds[1]. In earlier work[2,3] we have obtained several substituted pyrazoles and triazoles by cycloaddition of diazo compounds, sydnones, and p-methoxyphenyl azide to methyl 4,4-dimethoxy-2-butynoate (**1**) and to the corresponding nitrile, as representative examples of the relatively little studied 4-oxo-2-butynoic acid derivatives[4].

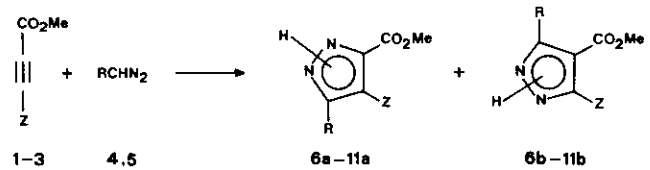
In the present paper we extend our study to the behaviour of methyl 4-oxo-2-butynoate (**2**) and methyl 4-hydroxy-2-butynoate (**3**) towards the above mentioned 1,3-dipoles. The results provide information on the influence of the substituent Z in unsymmetrical acetylenes **1-3** upon the reactivity and regioselectivity of the cycloadditions. Furthermore, the resulting pyrazoles and triazoles are appropriately functionalized and may serve as versatile synthetic intermediates suitable for the construction of new fused heterocyclic systems.

Although earlier attempts to obtain methyl 4-oxo-2-butynoate (**2**) by hydrolysis of the acetal-ester **1** under a variety of conditions were unsuccessful[4], we have now prepared **2** by formolysis of **1**, in analogy with a method previously reported by Gorgues for the preparation of acetylenedicarbaldehyde[5-7].

CYCLOADDITION OF DIAZO COMPOUNDS

Cycloaddition of diazomethane (**4**) and ethyl diazoacetate (**5**) to the acetylenic esters **1-3** afforded the pyrazoles **6-11**. The reactions proceed readily and the

pyrazoles are obtained in good yields. The only exception was found with formylpyrazoles **7a** and **7b**, in which the instability of compound **7b** and the competing side-reactions reduce greatly the yield. The reaction conditions and the ratio of regioisomers, estimated from the ^{1}H-nmr of the crude reaction mixtures, are summarized in Table 1.



1–3 4,5 6a–11a 6b–11b

Table 1. Cycloaddition of diazo compounds to the acetylenic esters **1-3**

Dipolarophile No.	Z	Dipole No.	R	Time h	Temperature °C	Products (ratio)	Yield %
1	$CH(OMe)_2$	**4**	H	4	0	**6a** (100:0)	92[a]
2	CHO	**4**	H	0.1	0	**7a+7b**[b]	-[c]
2	CHO	**4**	H	0.5	-70	**7a+7b** (60:40)[d]	-[c]
3	CH_2OH	**4**	H	24	0	**8a** (100:0)	90
1	$CH(OMe)_2$	**5**	CO_2Et	72	20	**9a** (100:0)	95[e]
2	CHO	**5**	CO_2Et	8	20	**10a+10b** (35:65)	95
3	CH_2OH	**5**	CO_2Et	72	20	**11a+11b** (95:5)	89

[a] Data from reference[2]. [b] Complex mixture which also contained N-methylpyrazoles and unidentified side-products. [c] Not estimated. [d] Approximate ratio estimated from the ^{1}H-nmr of the crude reaction mixture, which also contained other unidentified side-products. [e] Data from reference[3].

The ester-aldehyde **2** is much more reactive than the acetylenic esters **1** and **3** in 1,3-dipolar cycloadditions with diazo compounds. The reactions with the ester-acetal **1** and the ester-alcohol **3** occur with almost complete regiospecificity and show the expected orientation, which is determined by the electronic influence of the CO_2Me group. In contrast, both regioisomeric pyrazoles were formed with the ester-aldehyde **2**. The greater reactivity of **2** and the differences observed in the regiochemistry compared to **1** and **3** can be ascribed to the presence of a second strongly electron-withdrawing group attached to the alkyne[8].

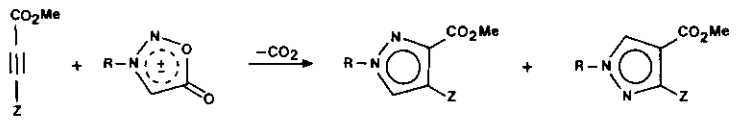
When the cycloaddition of diazomethane to the ester-aldehyde **2** was conducted in the presence of methanol or ethanol, the reaction resulted in the exclusive formation of the pyrazole **7a**, which was obtained in 90% yield. This fact may be rationalized in terms of the easy formation of the hemiacetal of **2**[9], the behaviour of which is similar to that of the ester-acetal **1**.

The structures of the formylpyrazoles were established by comparison of their spectral data with those of the pyrazoles **7a** and **10a** obtained by hydrolysis of their acetals **6a**[2] and **9a**[3], respectively. Structural assignments of the hydroxymethylpyrazoles **8a** and **11a**, obtained as the sole or the major product in the cycloadditions, were made by pyridinium chlorochromate oxidation of the

alcohols to the corresponding aldehydes, which were identical with the formylpyrazoles **7a** and **10a**, respectively.

CYCLOADDITION OF SYDNONES

A smooth reaction was also observed in the addition of N-benzyl- and N-phenylsydnones **12** and **13**, acting as azomethine imines, to the acetylenic esters **1-3** in refluxing toluene. The cycloaddition was followed by carbon dioxide evolution and aromatization to afford the pyrazoles **14-19** in good yields. The experimental conditions and the ratios of regioisomers are indicated in Table 2.



1-3 **12,13** **14a-19a** **14b-19b**

Table 2. Cycloaddition of sydnones to the acetylenic esters **1-3**

Dipolarophile No.	Z	Dipole No.	R	Time h	Temperature °C	Products (ratio)	Yield %
1	$CH(OMe)_2$	**12**	Bn	72	110	**14a+14b** (81:19)	80[a]
1	$CH(OMe)_2$	**13**	Ph	60	110	**15a+15b** (79:21)	84[a]
2	CHO	**12**	Bn	18	110	**16a+16b** (28:72)	90
2	CHO	**13**	Ph	18	110	**17a+17b** (34:66)	93
3	CH_2OH	**12**	Bn	72	110	**18a+18b** (50:50)	75
3	CH_2OH	**13**	Ph	48	110	**19a+19b** (40:60)	79

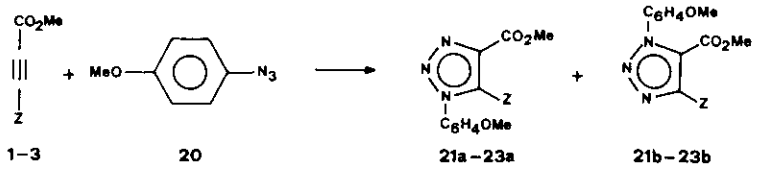
[a] Data from reference[3].

As can be seen in Table 2, the ester-aldehyde **2** is the most reactive dipolarophile, and the cycloaddition to sydnones **12** and **13** proceeds with inverse regioselectivity with respect to the ester-acetal **1**. Moreover, substitution of the acetal group in **1** by the CH_2OH substituent clearly lowers regioselectivity. The assignment of structure to the formylpyrazoles **16** and **17** was made by comparison of their spectral data with those of the aldehydes obtained by hydrolysis of the corresponding acetals[3]. The structures of the regioisomeric hydroxymethylpyrazoles **18** and **19** were established on the basis of the chemical shifts of the pyrazole protons, which in the regioisomers of type **b** resonate at lower field than in those of type **a**, as a consequence of the deshielding effect of the methoxycarbonyl group.

CYCLOADDITION OF p-METHOXYPHENYL AZIDE

Cycloaddition of the azide **20** to the alkynic dipolarophiles **1-3** afforded the triazoles **21-23** in high yields. Only with the ester-acetal **1** the reaction occurs

in a regiospecific manner, while esters **2** and **3** give isomer mixtures with low regioselectivity. The results and experimental conditions are summarized in Table 3.



1-3 **20** **21a-23a** **21b-23b**

Table 3. Cycloaddition of p-methoxyphenyl azide to the acetylenic esters **1-3**

Dipolarophile No.	Z	Time days	Temperature °C	Products (ratio)	Yield %
1	$CH(OMe)_2$	75	20	**21a** (100:0)	90[a]
2	CHO	30	20	**22a+22b** (36:64)	95
3	CH_2OH	60	20	**23a+23b** (66:34)	90

[a] Data from reference[3].

As in the above cases, the reactivity of the ester-aldehyde **2** towards the azide **20** is greater than with the ester-acetal **1** or with the ester-alcohol **3**. The results obtained on the regioselectivity of the cycloadditions with the azide **20** parallel those observed with sydnones.

The assignment of structure to the major regioisomer **23a** was made by chemical correlation; its oxidation with pyridinium chlorochromate yielded a formyl-triazol, the physical and spectral data of which were identical with those of **22a**, obtained by formolysis of methyl 1-p-methoxyphenyl-5-dimeythoxymethyl-1,2,3-triazole-4-carboxylate (**21a**)[3].

In summary, the results described in this study indicate that the ester-acetal **1** adds regiospecifically to diazo compounds and to the azide **20** and that the reaction of this same dipolarophile with sydnones occurs with high regio-selectivity. Likewise, the ester-alcohol **3** shows the greatest regioselectivity with diazo compounds, whereas in the reaction of **3** with the azide **20**, and specially with sydnones, a decrease in regiocontrol is observed. In contrast, cycloadditions of the ester-aldehyde **2** with the above mentioned 1,3-dipoles proceed in all cases with low regioselectivity and the regiochemistry is opposite to that obtained with **1** or **3**.

Moreover, comparison of the observed reaction times (see Tables 1-3) shows that the ester-aldehyde **2** is much more reactive than the esters **1** and **3** towards diazo compounds, sydnones and the azide **20**. However, in spite of the observed differences on reactivity, all cycloadditions give nearly complete reactions and the corresponding pyrazoles and triazoles are obtained in good to very good yields (75-95%).

EXPERIMENTAL

Mps are uncorrected. Ir spectra were recorded on a Perkin-Elmer model 257 grating spectrophotometer (ν_{max}, cm^{-1}). ^{1}H-Nmr spectra were obtained on a Varian EM-390 spectrometer for $CDCl_3$ solutions, using TMS (δ=0 ppm) as internal reference. Mass spectra were determined on a Hitachi-Perkin-Elmer model RMU-6MG spectrometer. Silica gel Merck 60 (70-230 mesh), DC-Alufolien 60 F_{254}, and F_{254} (2 mm layers) were used for column, analytical tlc, and preparative layer chromatography, respectively.

Methyl 4-oxo-2-butynoate (2)

A mixture of methyl 4,4-dimethoxy-2-butynoate (**1**)[4] (3.2 g, 20 mmol) and 99-100% formic acid (20 ml) was heated at 50 °C for 2 h. After removal of formic acid and ethyl formate in a rotary evaporator (temperature below 50 °C), the remaining oil was distilled to yield **2**, bp 38-40 °C/2 mm Hg (60%). Ir (film): 2265 (C≡C), 1720 (C=O ester); 1680 (C=O aldehyde). ^{1}H-Nmr : 9.30 (s, 1H, CHO); 3.86 (s, 3H, $COOCH_3$).

Cycloaddition of Diazomethane. General Procedure

To a solution of the acetylenic ester (2 mmol) in diethyl ether (5-10 ml) cooled at 0 °C, was added an ethereal solution of diazomethane (4 ml, containing 0.6 mmol/ml). The mixture was kept at 0 °C during the time indicated in Table 1. The solvent was removed and the residue analyzed by ^{1}H-nmr (Table 1).

Cycloaddition to 2.- a) The crude product obtained following the general procedure was a mixture of the pyrazoles **7a**[2], **7b**, and their N-methyl derivatives along with a variable amount of unidentified compounds. The methyl 3-formylpyrazole-4-carboxylate (**7b**) is unstable and was only identified by the ^{1}H-nmr spectrum of the crude mixture [10.57 (s, 1H, CHO); 8.28 (s, 1H, C-5); 4.00 (s, 3H, $COOCH_3$)]. b) The addition of diazomethane to **2**, at -70 °C using a 1.1:1 alkyne/diazomethane ratio, afforded a mixture containing the pyrazoles **7a** and **7b** in a ratio of *ca.* 60:40, the starting alkyne **2** and small amounts of unidentified products. c) When the cycloaddition of diazomethane to the ester-aldehyde **2** was carried out in methanol (or in diethyl ether impurified by ethanol) as solvent, only the pyrazole **7a**[2] (90%) was obtained.

Cycloaddition to 3.- The crude product was recrystallized from benzene (or chloroform) to yield the pyrazole **8a** (90%).

Methyl 4-hydroxymethylpyrazole-3-carboxylate (8a): mp 146-147 °C (Found: C, 45.99; H, 5.03; N, 18.28. Calcd for $C_6H_8N_2O_3$: C, 46.15; H, 5.12; N, 17.94. Ir (nujol): 3400, 3240 (NH, OH); 1700 (C=O). ^{1}H-Nmr: 7.59 (s, 1H, C-5); 4.75 (s, 2H, CH_2OH); 3.96 (s, 3H, $COOCH_3$). Ms, m/z: 156 (M^+), 123 (100%).

Cycloaddition of Ethyl Diazoacetate. General Procedure

To a solution of the acetylenic ester (2 mmol) in diethyl ether (5-10 ml) was added ethyl diazoacetate (228 mg, 2 mmol) and the mixture was allowed to stand at room temperature during the period indicated in Table 1. The solvent was removed and the residue was analyzed by ^{1}H-nmr.

Cycloaddition to 2.- The crude product was a mixture of the pyrazoles **10a**[3] and

10b (95%) in a 35:65 ratio. Attempts to separate the pyrazoles **10a** and **10b** by chromatography on silica gel were unsuccessful. The mixture was acetalized with methyl orthoformate, in the presence of methanol and p-toluenesulfonic acid to yield the regioisomeric acetals **9a**[3] and **9b**, which were isolated by preparative tlc (benzene-acetone 8:1).

Ethyl 5-dimethoxymethyl-4-methoxycarbonylpyrazole-3-carboxylate (9b). Lower Rf component (Found: C, 48.40; H, 5.80; N, 10.42. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92; N, 10.29). Ir (film): 3230 (NH); 1730 (C=O). ^{1}H-Nmr: 5.80 (s, 1H, acetal); 4.39 (q, 2H, OCH_2, J=7.0 Hz); 3.85 (s, 3H, $COOCH_3$); 3.37 (s, 6H, OCH_3); 1.36 (t, 3H, $CH_2\underline{CH}_3$, J=7.0 Hz). Ms, m/z: 272 (M^+).

Ethyl 5-formyl-4-methoxycarbonylpyrazole-3-carboxylate (10b): A solution of the acetal **9b** (150 mg) in 99-100% formic acid (5 ml) was allowed to stand for 4 h at room temperature and then water (25 ml) was added. After thorough extraction with diethyl ether, washing of the combined organic layers with water and driyng ($MgSO_4$), the aldehyde **10b** was obtained, mp 149-151 °C (from cyclohexane). (Found: C, 47.50; H, 4.48; N, 12.29. Calcd for $C_9H_{10}N_2O_5$: C, 47.78; H, 4.42; N, 12.38. Ir (nujol): 3400 (NH); 1750, 1690 (C=O). ^{1}H-Nmr: 10.14 (s, 1H, CHO); 4.33 (q, 2H, OCH_2, J=7.0 Hz); 3.93 (s, 3H, $COOCH_3$); 1.37 (t, 3H, $CH_2\underline{CH}_3$, J=7.0 Hz). Ms, m/z: 227 (M^++1), 167 (100%).

Cycloaddition to 3.- The crude product was chromatographed on silica gel (benzene-ethyl acetate 1:1) to yield the pyrazoles **11a** and **11b** (89%) in a 95:5 ratio.

Ethyl 4-hydroxymethyl-5-methoxycarbonylpyrazole-3-carboxylate (11a): Higher Rf component, mp 105-106 °C (from benzene). (Found: C, 47.26; H, 5.46; N, 12.57. Calcd for $C_9H_{12}N_2O_5$: C, 47.36; H, 5.30; N, 12.27). Ir (nujol): 3340 (NH, OH); 1730 (C=O). ^{1}H-Nmr: 5.12 (s, 2H, CH_2OH); 4.50 (q, 2H, OCH_2, J=7.0 Hz); 4.00 (s, 3H, OCH_3); 1.40 (t, 3H, $CH_2\underline{CH}_3$, J=7.0 Hz). Ms, m/z: 228 (M^+), 181 (100%), 167.

Ethyl 5-hydroxymethyl-4-methoxycarbonylpyrazole-3-carboxylate (11b): mp 87-89 °C (from ethyl acetate-petroleum ether). (Found: C, 46.98; H, 4.81; N, 11.98. Calcd for $C_9H_{12}N_2O_5$: C, 47.36; H, 5.30; N, 12.27). Ir (KBr): 3440, 3190 (NH, OH); 1750, 1720 (C=O). ^{1}H-Nmr: 4.99 (s, 2H, CH_2OH); 4.44 (q, 2H, OCH_2, J=7.0 Hz); 3.88 (s, 3H, OCH_3); 1.35 (t, 3H, $CH_2\underline{CH}_3$, J=7.0 Hz). Ms, m/z: 228 (M^+), 196 (100%), 167.

Cycloaddition of Sydnones. General Procedure

To a solution of the acetylenic ester (2 mmol) in toluene (5 ml) was added the sydnone (1.5 mmol). The cycloadditions of benzylsydnone were conducted in the presence of a small amount of 2,5-di-tert-butyl-p-cresol, as free radical inhibitor to prevent the sydnone decomposition. The reaction mixture was heated under reflux during the period indicated in Table 2. The solvent was removed in vacuo and the residue was analyzed by ^{1}H-nmr. The crude product was chromatographed on silica gel (benzene-ethyl acetate 4:1).

Cycloaddition to 2.- The reaction with benzylsydnone **12** afforded a mixture of the pyrazoles **16a** and **16b** (90%) in a 28:72 ratio. The addition of phenylsydnone (**13**) yielded the pyrazoles **17a** and **17b** (93%) in a 34:66 ratio. The pyrazoles **16a,b** and **17a,b** were identical with those previously reported[3].

Cycloaddition to 3.- The addition of benzylsydnone afforded the pyrazoles **18a**

and **18b** (75%) in a 50:50 ratio.The reaction with phenylsydnone yielded a mixture of the pyrazoles **19a** and **19b** (79%) in a 40:60 ratio.

Methyl 1-benzyl-4-hydroxymethylpyrazole-3-carboxylate (18a): Lower Rf component, mp 31-33 °C (from benzene-cyclohexane). (Found: C, 63.62; H, 5.79; N, 11.31. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.41; H, 5.69; N, 11.38). Ir (film): 3410 (OH); 1725 (C=O). ^{1}H-Nmr: 7.45-7.30 (m, 5H, arom., and 1H, C-5); 5.37 (s, 2H, CH_2); 4.65 (br s, 2H, $C\underline{H}_2OH$); 3.97 (s, 3H, OCH_3). Ms, m/z: 246 (M^+), 91 (100%).

Methyl 1-benzyl-3-hydroxymethylpyrazole-4-carboxylate (18b): mp 61-63 °C (from benzene-cyclohexane). (Found: C, 63.42; H, 5.74; N, 10.99. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.41; H, 5.69; N, 11.38). Ir (film): 3450 (OH); 1730 (C=O). ^{1}H-Nmr: 7.87 (s, 1H, C-5); 7.40 (m, 5H, arom.); 5.32 (s, 2H, CH_2); 4.80 (br s, 2H, $C\underline{H}_2OH$); 3.85 (s, 3H, OCH_3). Ms, m/z: 246 (M^+), 229, 91 (100%).

Methyl 1-phenyl-4-hydroxymethylpyrazole-3-carboxylate (19a): Lower Rf component, mp 93-94 °C (from benzene). (Found: C, 61.89; H, 5.11; N, 11.85. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.05; H, 5.20; N, 12.06). Ir (nujol): 3360 (OH); 1730, 1710 (C=O). ^{1}H-Nmr: 8.05 (s, 1H, C-5); 7.80-7,40 (m, 5H, arom.); 4.89 (br s, 2H, CH_2OH); 4.05 (s, 3H, OCH_3). Ms, m/z: 232 (M^+), 77 (100%).

Methyl 1-phenyl-3-hydroxymethylpyrazole-4-carboxylate (19b): mp 91-92 °C (from benzene) . (Found: C, 62.19; H, 5.22; N, 12.26. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.05; H, 5.20; N, 12.06). Ir (nujol): 3440, 3320 (OH); 1710 (C=O). ^{1}H-Nmr: 8.50 (s, 1H, C-5); 7.80-7.40 (m, 5H, arom.); 4.95 (d, 2H, $C\underline{H}_2OH$, J=6.0 Hz); 3.95 (s, 3H, OCH_3). Ms, m/z: 232 (M^+), 77 (100%).

Cycloaddition of p-Methoxyphenyl azide. General Procedure

To a solution of the acetylenic ester (2.5 mmol) in diethyl ether or benzene (10 ml) was added the azide (2 mmol) and the reaction mixture was kept in the dark, at room temperature, for the time indicated in Table 3. After removing the solvent, the residue was analyzed by ^{1}H-nmr.

Cycloaddition to 2.- The crude product was a mixture containing the triazoles **22a** and **22b** (95%) in a 36:64 ratio. Attempts to separate the triazole aldehydes by chromatography on silica gel were unsuccessful. The crude mixture was acetalized with methanol and sulfuric acid as a catalyst to afford the acetals **21a**[3] and **21b**, which were isolated by tlc (petroleum ether-ethyl acetate 1:1).

Methyl 1-p-methoxyphenyl-4-dimethoxymethyl-1,2,3-triazole-5-carboxylate (21b): Lower Rf component, mp 58-59 °C (from cyclohexane). (Found: C, 54.83; H, 5.67; N, 14.12. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.71; H, 5.57; N, 13.67). Ir (nujol): 1740 (C=O). ^{1}H-Nmr: 7.43-6.95 (m, 4H, arom.); 5.94 (s, 1H, acetal); 3.87, 3.84 (2s, 6H, OCH_3); 3.52 (s, 6H, OCH_3). Ms, m/z: 307 (M^+), 220, 75 (100%).

Methyl 1-p-methoxyphenyl-4-formyl-1,2,3-triazole-5-carboxylate (22b): To the acetal **21b** (150 mg) was added 99-100% formic acid (5 ml) and the reaction mixture was allowed to stand at room temperature for 6 h. Water was added (25 ml) and the solution was extracted thoroughly with diethyl ether. The solvent was removed and the residue was recrystallized from cyclohexane. Mp 107-108 °C. (Found: C, 55.51; H, 4.24; N, 16.21. Calcd for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.21; N, 16.09). Ir (nujol): 1745, 1700 (C=O). ^{1}H-Nmr: 10.32 (s, 1H, CHO); 7.46-6.96 (m, 4H, arom.); 3.92, 3.87 (2s, 6H, OCH_3). Ms, m/z: 261 (M^+), 146 (100%).

Cycloaddition to 3.- The crude product was a mixture of the triazoles **23a** and

23b (90%) in a 66:34 ratio. The triazoles were isolated by chromatography on silica gel (hexane-ethyl acetate 1:1).

Methyl 1-p-methoxyphenyl-5-hydroxymethyl-1,2,3-triazole-4-carboxylate (23a): Higher Rf component, mp 133 °C (from cyclohexane). (Found: C, 54.35; H, 4.80; N, 16.12. Calcd for $C_{12}H_{13}N_3O_4$: C, 54.75; H, 4.94; N, 15.96). Ir (nujol): 3300 (OH); 1730 (C=O). ^{1}H-Nmr: 7.50, 7.00 (m, 4H, arom.); 4.80 (d, 2H, $C\underline{H}_2OH$, J=6.0 Hz); 4.04, 3.90 (2s, 6H, OCH_3); 3.97 (t, 1H, OH, J=6.0 Hz). Ms, m/z: 263 (M^+), 176 (100%).

Methyl 1-p-methoxyphenyl-4-hydroxymethyl-1,2,3-triazole-5-carboxylate (23b): mp 137-138 °C (from cyclohexane). (Found: C, 55.04; H, 5.04; N, 15.93. Calcd for $C_{12}H_{13}N_3O_4$: C,54.75; H, 4.94; N, 15.96). Ir (nujol): 3360, 3220 (OH); 1735 (C=O). ^{1}H-Nmr: 7.40-6.94 (m, 4H, arom.); 5.00 (d, 2H, $C\underline{H}_2OH$, J=6.0 Hz); 3.87, 3.82 (2s, 6H, OCH_3); 3.20 (t, 1H, OH, J=6.0 Hz). Ms, m/z: 263 (M^+), 176 (100%).

Oxidation of hydroxymethylazoles to formylazoles

A solution of the azole (**8a**, **11a** or **23a**, 1 mmol) in dry dichloromethane (3 ml) was added to a stirred suspension of pyridinium chlorochromate (150 mg) in dry dichlorochromate (5 ml). The mixture was stirred at room temperature for 2 h, then diethyl ether (5 ml) was added and the mixture was stirred until a gummy material appeared. The solution was filtered through a short column of Florisil which was further eluted with dichloromethane. The solvent was removed and the crude product was recrystallized (from water or cyclohexane) to afford the corresponding formylazoles (**7a**, **10a** or **22a**).

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