Molecular Rearrangements of 4-Iminomethyl-1,2,3-Triazoles. Replacement of 1-Aryl Substituents in 1*H*-1,2,3-Triazole-4-carbaldehydes

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The two structural isomers, **4** and **5**, of 1-substituted-4-iminomethyl-1,2,3-triazoles are interconvertible when heated in dimethyl sulfoxide at 80°. The equilibrium position depends on the electronic properties of the R-substituent, favoring **5** for R = alkyl, benzyl and anisyl, and **4** for *p*-chlorophenyl and *p*-nitrophenyl. An interesting application is the synthesis of 1-alkyl-1,2,3-triazole-4-carbaldehydes from 1-phenyl-1,2,3-triazole-4-carbaldehyde by Scheme I. The hydrazones **4i,j** and the oxime **4k** do not rearrange due to an unfavorable *Z*-configuration around the C=N bond, whereas the acyloximino derivative **4m** is converted into the nitrile **11**. The structures of the products have been fully characterized by ^{13}C nmr spectroscopy and the mechanistic details of the rearrangement are discussed.

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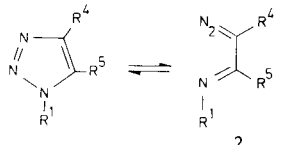
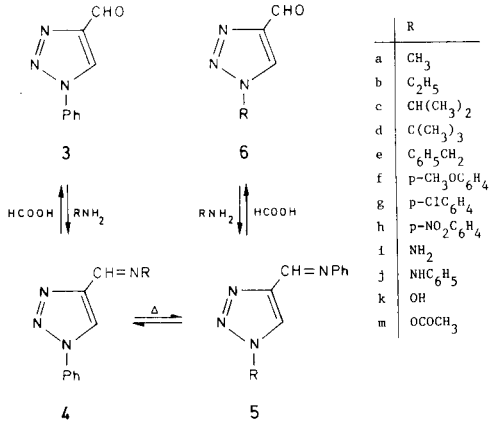
1*H*-1,2,3-Triazoles **1** can exist in thermal equilibrium with diazo-imines **2**, and this constitutes the basis of a series of molecular rearrangements involving the substituent at the 4- or 5-position. If the same ring system (triazole) is produced but with a different substitution pattern, the reaction is denoted as a ring-degenerate rearrangement [1]. This occurs, for instance, by thermolysis of 5-amino- [2], 5-hydrazino- [3] and 5-diazomethyl substituted triazoles [4].



1 2

Recent studies have shown that 4-iminomethyl substituted 1*H*-1,2,3-triazoles (**1**, R^4 = CH=NR) are also capable of undergoing a ring-degenerate rearrangement, since the intermediate diazo-imine **2** (R^4 = CH=NR) can cyclize in two directions. Rearrangements were observed when R^5 is a hydroxy [5], amine [6] or azide substituent [7]. The facility of this reaction prompted us to investigate the thermolysis of 4-iminomethyltriazoles bearing a hydrogen atom at the 5-position as a possible means of converting 1-aryltriazole-4-carbaldehydes into 1-alkyltriazole-4-carbaldehydes (see Scheme I). Although no rearrangements of 1*H*-1,2,3-triazoles with a hydrogen atom at the 5-position were known, ring opening reactions of such triazoles are feasible, and have indeed been reported when the N-1 substituent is strongly electron-withdrawing (*e.g.* CN) [8]. We now describe the first examples of rearrangements of 5-unsubstituted triazoles and their application in exchanging the N-1 substituent of 1,2,3-triazole-4-carbaldehydes [9] (Scheme I).

Scheme I



The iminomethyltriazoles **4a-e**, derived from the known aldehyde **3** [10] and alkylamines, were found to rearrange completely into the isomeric triazoles **5a-e** when heated at 80° in dimethyl sulfoxide (ethanol can also be used as solvent). These were hydrolyzed with 10-15% formic acid into the 1-alkyltriazole-4-carbaldehydes **6a-e**. The ready accessibility of **3** and the wide choice of amines, coupled with the ease of operation, make the sequence **3** → **4** → **5** → **6** an excellent method for the preparation of 1-alkyl-1,2,3-triazole-4-carbaldehydes. In particular, it allows the synthesis of sterically hindered derivatives such as **6d**, which would be difficult to obtain by the classical 1,3-dipolar cycloaddition reaction of the corresponding azide with propiolaldehyde. Furthermore, our method offers the advantage of using the safe phenyl azide instead of the low-boiling explosive alkyl azides [11], necessary for the preparation of the lower alkyl derivatives, *e.g.* **6a,b**.

When R in **4** is an aryl group, the equilibrium position depends on the electron-donating or electron-withdrawing properties of the substituent. For instance, **4f** equilibrates with 59% of **5f** in dimethyl sulfoxide at 80°, whereas **4h** does not rearrange. This was verified by preparing **5h** from **6h** and converting it quantitatively into **4h**. The equilibrium positions of the above examples could readily be determined by integration of the CH=N and C_5-H re-

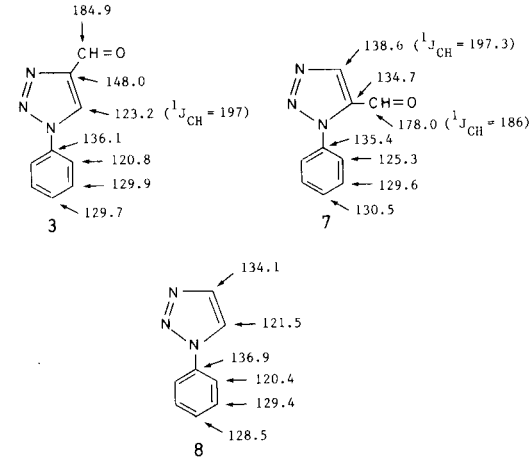
sonances in the 90 MHz ^1H nmr spectra, but the close proximity of these absorptions in **4g** and **5g** precluded quantitative analysis. In this case, however, **4g** is favored since it was isolated in crystalline form in 56% yield by thermolysis of **5g** (prepared from **6g** and aniline). The equilibrium concentration of **4g** was finally estimated at ca 70% by 250 MHz nmr measurements. From these experiments we conclude that the equilibrium **4** ⇌ **5** is shifted towards the triazole form possessing the strongest electron-withdrawing substituent at the imine nitrogen.

Finally, we have also prepared the hydrazones **4i,j** and the oxime **4k**, but no rearrangement was observed on heating them in dimethyl sulfoxide at 80°.

A detailed ^{13}C nmr analysis of the triazoles has been carried out and the data are listed in Tables 1 and 2. The isomerization of **4** into **5** is accompanied by a large downfield shift of the phenyl C_{ipso} ($\Delta\delta \simeq 15$ ppm) and a small upfield shift of the phenyl C_p ($\Delta\delta \simeq 3$ ppm), while the triazole C-4 (δ 146-148) and C-5 resonances (δ 120-124) are not much altered. They occur at positions similar to those found for the triazole-4-carbaldehydes **3** and **6**.

If we compare the ^{13}C nmr spectrum of **3** with that of the isomeric triazole-5-carbaldehyde **7** (Scheme II, deuteriochloroform as solvent), two important features are noticed. Firstly, the phenyl C_o-resonance of **7** is shifted downfield by 4.5 ppm compared with that of **3**; a phenomenon already reported by Begtrup [12] when a methyl or chloro substituent is introduced at the 5-position of 1-phenyltriazole. Secondly, the difference in chemical shifts between the C-4 and C-5 atoms is large in **3** ($\Delta\delta_{4,5}$ = 24.8) and small in **7** ($\Delta\delta_{4,5}$ = 3.9). This is due to the strong inductive effect of the formyl group on the α-carbon atom, which causes a large downfield shift of C-4 in **3** and of C-5 in **7** compared with the parent 1-phenyltriazole **8** [12] (see Scheme II).

Scheme II



If $Z_{i,j}$ denotes the influence of the formyl substituent in position i on the carbon resonance of position j, the following increments are calculated (the positive values correspond to downfield shifts):

Table 1

^{13}C Chemical Shifts of the triazole-4-carbaldehydes [a]

Compound	Solvent	C-4	C-5 ($^1J_{CH}$)	C=O ($^1J_{CH}$)	Phenyl or R (aryl) [b] C_i	C_o	C_m	C_p	C_{sp^3} ($^1J_{NCH}$)
3	$CDCl_3$	148.0	123.2 (198)	184.9	136.1	120.8	129.9	129.7	
6a	$CDCl_3$	148.0	126.1 (196)	184.9 (181.5)					37.0 (142.5)
6b	$CDCl_3$	147.8	124.4 (196)	185.1 (181.6)					15.2, 45.8 (142.5)
6c	$CDCl_3$	147.5	122.8 (196.3)	185.1 (181.3)					22.8, 53.6 (143)
6d	$CDCl_3$	147.2	122.7 (196)	185.4 (181)					29.8, 60.5
6e	$CDCl_3$	148.1	125.2 (197.5)	185.1 (181.5)	133.5	128.4	129.4	129.3	54.5 (143)
6f	$(CD_3)_2SO$	147.5	125.9 (201)	185.0 (182)	129.3	122.4	115.0	160.0	55.6
6g	$CDCl_3$	148.2	123.0 (198.3)	184.8 (183.1)	134.6	122.0	130.2	135.8	
6h	$(CD_3)_2SO$	147.9	126.9 (202)	185.0 (184)	140.4	121.6	125.6	147.4	

[A] The chemical shifts are given in ppm downfield from TMS and the $^1J_{CH}$ coupling constants (values in parentheses) are given in Hz. Other coupling constants are $^2J_{C4\text{-}CHO}$ = 24.5-26 Hz, $^2J_{C4\text{-}H5}$ = 9.5-9.7 Hz, $^3J_{C5\text{-}CHO}$ = 4-5 Hz. [b] C_i, C_o, C_m and C_p denote positions with respect to the triazole ring.

$Z_{44} = 13.9$ $Z_{45} = 1.7$

$Z_{55} = 13.2$ $Z_{54} = 4.5$

Thus, the α-effect of the formyl group in triazoles is similar to the α-effect in acrolein ($Z_\alpha = 15.3$) and much larger than that in benzaldehyde ($Z_\alpha = 8.2$), whereas the reverse is true for the β-effect ($Z_\beta = 14.5$ for acrolein and 1.2 for benzaldehyde) [13].

The triazole-4-imines which undergo rearrangement **(4a-g, 5h)** all possess the expected *E*-configuration about the C=N bond. This is evidenced by the magnitude of the one-bond $^{13}CH=N$ coupling constants, ^1J = 161-165 Hz, which would be larger for the *Z*-isomers (*ca* 177 Hz) [14]. The cis-relationship between the triazole and the imine-nitrogen lone pair is a necessary condition for rearrangement. Indeed, following the mechanistic study of the azidoazomethine-1*H*-tetrazole isomerization based on ab-initio calculations [15], the ring closure of diazo-imines **2**

Table 2
^{13}C Chemical Shifts of the 4-Iminomethyltriazoles [a]

Compound	Solvent	C-4	C-5 ($^1J_{CH}$)	CH=N ($^1J_{CH}$)	Phenyl				R (aryl) [b]				C_{sp}^3 ($^1J_{NCH}$)
					C_i	C_o	C_m	C_p	C_i	C_o	C_m	C_p	
4a	$CDCl_3$	147.1	120.1 (196)	154.5 (162)	136.8	120.6	129.8	129.1					48.3 (134.5)
4b	$CDCl_3$	147.1	120.2 (197)	152.5 (162.2)	136.8	120.5	129.8	129.0					16.0, 55.9 (134.5)
4c	$CDCl_3$	147.0	120.3 (197)	150.5 (162)	136.7	120.4	129.7	128.9					23.9, 61.8
4d	$CDCl_3$	148.0	119.9 (196.5)	148.0 (161)	136.8	120.5	129.7	128.9					29.5, 58.0
4e	$CDCl_3$	146.9	120.5 (197)	153.8 (162)	136.6	120.5	129.8	129.0	138.4	128.1	128.5	127.2	65.3 (134.5)
4f	$CDCl_3$	147.7	120.6 (197)	149.5 (163)	136.7	120.6	129.8	129.1	143.9	122.2	114.5	158.8	55.4
4g	$(CD_3)_2SO$	146.5	123.3 (200.7)	152.6 (165)	136.3	120.4	130.0	129.2	149.6	122.9	129.3	130.8	
4h	$(CD_3)_2SO$	146.1	123.9 (201)	154.9 (166.2)	136.1	120.4	129.8	129.1	156.7	121.8	124.9	145.1	
4i	$(CD_3)_2SO$	142.4	121.6 (199)	122.9 (183)	136.3	120.4	129.9	129.0					
4j	$(CD_3)_2SO$	142.9	122.7 (200)	121.7 (184)	136.1	120.5	129.9	129.2	144.5	112.6	129.1	119.9	
4k	$(CD_3)_2SO$	138.4	125.5 (205)	137.3 (180)	136.3	120.6	129.8	128.9					
4m	$CDCl_3$	140.2	120.9 (198)	148.4 (172)	136.4	120.6	129.9	129.4					19.3, (CO at 168.0)
5a	$CDCl_3$	147.2	124.0 (195)	152.0 (163)	151.3	120.8	129.2	126.5					36.9 (142)
5b	$CDCl_3$	146.9	122.4 (195.5)	152.1 (164)	151.2	120.7	129.2	126.4					15.3, 45.5 (142)
5c	$CDCl_3$	146.7	120.6 (196)	152.4 (163)	151.3	120.8	129.2	126.4					22.9, 53.3 (142)
5d	$CDCl_3$	146.2	120.3 (195)	152.6 (163)	151.3	120.8	129.2	126.3					29.9, 60.0
5e	$CDCl_3$	147.2	122.9 (196)	152.0 (164)	151.1	120.7	129.2	126.4	133.9	128.4	129.2	129.0	54.5
5f	$(CD_3)_2SO$	146.4	122.7 (200)	151.8 (163)	150.9	120.8	129.2	126.2	129.6	121.9	114.8	159.5	55.5
5g	$(CD_3)_2SO$	146.7	123.0 (201)	151.6 (164.6)	150.7	120.9	129.2	126.4	135.0	122.0	129.8	133.4	
5h	$(CD_3)_2SO$	147.0	123.4 (202)	151.3 (165.5)	150.6	120.9	129.2	126.5	140.4	120.9	125.4	146.9	

[a] The chemical shifts are given in ppm downfield from TMS and the $^1J_{CH}$ coupling constants (values in parentheses) are given in Hz. Other coupling constants are: $^2J_{C\text{-}4\text{-}H}$ = 9-10.5, $^3J_{C\text{-}5\text{-}CHN}$ = 4.5-5Hz. [b] C_i, C_o, C_m and C_p denote positions with respect to the triazole ring or imine nitrogen.

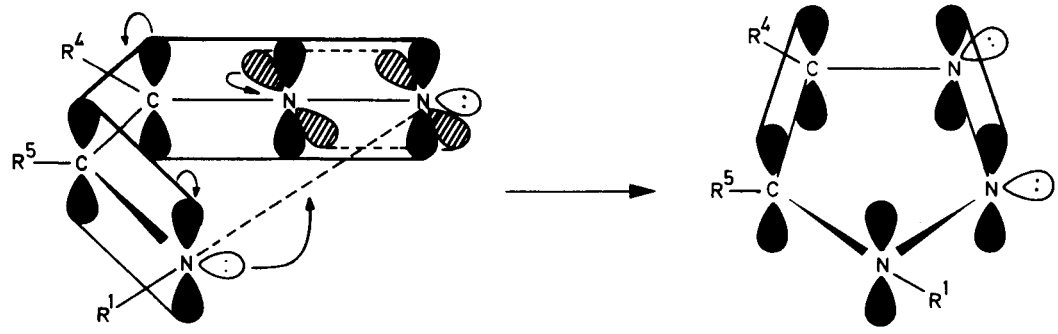
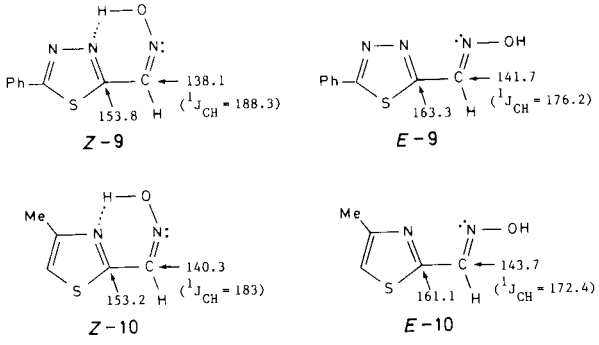


Figure 1. Electronic reorganization during the ring-closure of a diazo-imine.

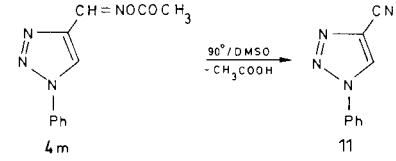
can be depicted as shown in Figure 1. Thus, the cyclization reaction proceeds by a bending of the diazo function, due to the formation of a lone electron pair on the central nitrogen atom. This is accompanied by a π-electron flow towards the imine function and the formation of a σ-bond at the expense of the lone pair on the imine nitrogen.

In the light of this mechanism, the reluctance of the hydrazones **4i,j** and the oxime **4k** to rearrange is explained by their unfavorable *Z*-configuration, due to intramolecular hydrogen bonding with the triazole N-3 atom. This conclusion is confirmed by comparison of the $^{13}CH=N$ coupling constants, $^1J_{CH}$ = 180-184 Hz, with those of two reference compounds **9** and **10** which were available in both stereoisomeric structures (Scheme III, dimethyl sulfoxide-d_6 as solvent) [16]. Furthermore, the triazole C-4 absorptions of **4i-k** are shifted upfield by 6-10 ppm compared with the aldehyde **3** (see Tables 1 and 2). This γ-effect is also present in our model compounds ***Z*-9** and ***Z*-10**, where the resonances of the C-2 atoms occur at higher fields than those in the *E*-isomers or the corresponding aldehydes (δ 166.7 and 165.1).

Scheme III



In order to promote *Z-E* equilibration of **4k** and to facilitate its conversion to **5k** [17], the *O*-acetyl derivative **4m** was prepared and then heated in dimethyl sulfoxide at 90°. Instead of **5k**, the nitrile **11** was obtained in analogy with the elimination decomposition of other aldoximes [18].



EXPERIMENTAL

1-Phenyl-1,2,3-triazole-4-carbaldehyde (**3**).

This compound has been prepared from phenyl azide and propiolaldehyde or the corresponding diethyl acetal [10]. A more convenient synthesis is as follows:

A solution of propargyl alcohol (11 g, 0.19 mole) and phenyl azide (23 g, 0.19 mole) was refluxed in toluene (500 ml) for 18 hours. The solvent was removed *in vacuo* and the residue was crystallized from chloroform-ether to give 4-hydroxymethyl-1-phenyl-1,2,3-triazole in 76% yield (25.3 g), mp 105°. Note: The 1,5-isomer was also formed as minor component (20% by ^1H nmr) but remained in solution.

The 4-hydroxymethyltriazole (5 g, 30 mmoles) and freshly prepared manganese dioxide (24 g, 0.3 mole) was stirred overnight in dichloromethane (250 ml) at room temperature. After filtration of the reaction mixture, the solvent was evaporated *in vacuo* and the residue crystallized from chloroform-ether to give **3** in 80% yield (4.2 g), mp 96° (lit [10] 99°); ir (potassium bromide): 3140 (m, =CH), 1690 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 7.5-7.9 (two m, 5H, Ph), 8.6 (s, 1H, triazole H), 10.2 (s, 1H, CHO).

Anal. Calcd. for $C_9H_7N_3O$ (mol wt 173): C, 62.42; H, 4.07. Found: C, 62.33; H, 4.11.

1-Methyl-1,2,3-triazole-4-carbaldehyde (**6a**).

To a solution of **3** (1 g, 5.8 mmoles) in methanol (20 ml) was added an aqueous solution (40%) of methylamine (1 ml, 2 equivalents), and the whole was stirred overnight at room temperature. The solvent was removed *in vacuo* and the resulting oil was dissolved in chloroform, washed with water and dried over magnesium sulfate. The solvent was evaporated to give **4a** in 74% yield (0.8 g), mp 87° (ether-petroleum ether).

Anal. Calcd. for $C_{10}H_{10}N_4$ (mol wt 186): C, 64.50; H, 5.41.

Found: C, 64.64; H, 5.47.

This compound (0.42 g, 2.2 mmoles) was heated overnight in dimethyl sulfoxide (4 ml) at 80°. The solution was poured into ice-water and the precipitated **5a** (0.2 g) was collected by filtration. The filtrate was extracted with chloroform, and the extracts were dried over magnesium sulfate and evaporated to give another crop of **5a** (0.2 g), overall yield 95% (0.4 g), mp 154° (ether-petroleum ether).

Compound **5a** (0.2 g, 1.1 mmoles) was dissolved in a mixture of water-methanol (15 ml, 1:1) containing 15% of formic acid and the solution was heated overnight at 80°. After cooling, the reaction mixture was poured into water and extracted with chloroform to remove side-products. The water layer was neutralized with sodium bicarbonate and then extracted with dichloromethane. The extracts were dried over magnesium sulfate and evaporated to give **6a** in 67% yield (0.08 g), mp 113° (chloroform-ether) (lit [19] 113°); ir (potassium bromide): 1690 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 4.1 (s, 3H, CH_3), 8.07 (s, 1H, triazole H), 10.1 (s, 1H, CHO).

1-Ethyl-1,2,3-triazole-4-carbaldehyde (**6b**).

To a solution of **3** (1 g, 5.8 mmoles) in methanol (20 ml) was added an aqueous solution (70%) of ethylamine (0.57 ml, 1.5 equivalents), and the whole was stirred overnight at room temperature. The solution was concentrated and the resulting precipitate **4b** was filtered off and dried, yield 52% (0.6 g), mp 35° (petroleum ether).

This compound (0.6 g, 3 mmoles) was heated overnight in dimethyl sulfoxide (2 ml) at 80°. The solution was poured into ice-water and the precipitate **5b** was collected in 83% yield (0.5 g), mp 83° (ethanol).

Anal. Calcd. for $C_{11}H_{12}N_4$ (mol wt 200): C, 65.98; H, 6.04. Found: C, 66.06; H, 5.91.

Compound **5b** (0.5 g, 2.5 mmoles) was dissolved in a mixture of water-methanol (20 ml, 1:1) containing 10% of formic acid and the solution was heated overnight at 80°. After addition of water (20 ml), the solution was extracted with chloroform and the extracts were washed with water and dried over magnesium sulfate. The solvent was removed and the resulting oil (0.3 g) was chromatographed on silica gel with dichloromethane-ether (9:1) as the eluent to give **6b** in 48% yield (0.15 g); ir (neat) 1700 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 1.6 (t, 3H, CH_3), 4.5 (q, 2H, CH_2), 8.15 (s, 1H, triazole H), 10.15 (s, 1H, CHO). This compound was identical (ir, ^1H nmr) with an authentic sample prepared from propiolaldehyde and ethyl azide.

1-Isopropyl-1,2,3-triazole-4-carbaldehyde (**6c**).

A solution of **3** (0.5 g, 2.9 mmoles) and two equivalents of isopropylamine (0.35 g) in methanol (10 ml) was stirred overnight at room temperature. After replacement of methanol by chloroform, the solution was washed with water and dried over magnesium sulfate. The solvent was evaporated to give **4c** as an oil in 74% yield (0.46 g).

This compound (0.4 g, 1.9 mmoles) was heated overnight in dimethyl sulfoxide (3 ml) at 80°. The solution was poured into ice-water, extracted with chloroform, washed with water and evaporated. The resulting oil **5c** was dissolved in a mixture of water-methanol (20 ml, 1:1) containing 15% of formic acid and heated overnight at 80°. After addition of water (20 ml), the solution was extracted with chloroform and the extracts were washed with water and dried over magnesium sulfate. The solvent was removed and the resulting oil (0.22 g) was chromatographed on silica gel with dichloromethane-ether (9:1) as the eluent, giving **6c** in 34% yield (0.09 g); ir (neat): 1700 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 1.6 (d, 6H, two Me), 4.9 (sept, 1H, isopropyl), 8.15 (s, 1H, triazole H), 10.15 (s, 1H, CHO). This compound was identical (ir, ^1H nmr) with an authentic sample prepared from propiolaldehyde and isopropyl azide.

1-*t*-Butyl-1,2,3-triazole-4-carbaldehyde (**6d**).

A solution of **3** (1 g, 5.8 mmoles) and two equivalents of *t*-butylamine (0.84 g) in methanol (20 ml) was stirred overnight at room temperature. After removal of the solvent, **4d** was obtained as an oil in 93% yield (1.23 g).

This compound (1 g, 4.4 mmoles) was heated overnight in dimethyl sulfoxide (4 ml) at 80°. Then the solution was poured into ice-water and the precipitate **5d** was collected in 74% yield (0.74 g), mp 105° (ethanol).

Anal. Calcd. for $C_{13}H_{16}N_4$ (mol wt 288): C, 68.39; H, 7.06. Found: C, 68.22; H, 6.93.

Compound **5d** (0.47 g, 2.06 mmoles) was dissolved in a mixture of water-methanol (20 ml, 1:1) containing 10% of formic acid and the whole was refluxed overnight. After addition of water (20 ml), the solution was extracted with chloroform and the extracts were washed with water and dried over magnesium sulfate. The solvent was removed and the resulting oil (0.38 g) was chromatographed on silica gel with ether as the eluent, giving **6d** as an oil in 52% yield (0.18 g); ir (neat) 1700 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 1.75 (s, 9H, three Me), 8.3 (s, 1H, triazole H), 10.15 (s, 1H, CH=O).

Anal. Calcd. for $C_7H_{11}N_3O$ (mol wt 187): C, 54.89; H, 7.24. Found: C, 54.78; H, 7.16.

1-Benzyl-1,2,3-triazole-4-carbaldehyde (**6e**).

A solution of **3** (1 g, 5.8 mmoles) and two equivalents of benzylamine (1.2 g) in methanol (40 ml) was stirred at room temperature for 1 day. The solution was concentrated and cooled to give **4e** in 84% yield (1.28 g), mp 111° (ethanol).

Anal. Calcd. for $C_{16}H_{14}N_4$ (mole wt 262): C, 73.26; H, 5.38. Found: C, 73.40; H, 5.37.

This compound (1 g, 3.8 mmoles) was heated in dimethyl sulfoxide (6 ml) at 80° for 16 hours. After cooling, the solution was poured into ice-water and the precipitate **5e** was collected in 90% yield (0.9 g), mp 120° (ethyl acetate).

Anal. Calcd. for $C_{16}H_{14}N_4$ (mol wt 262): C, 73.26; H, 5.38. Found: C, 73.23; H, 5.36.

Compound **5e** (0.9 g, 3.44 mmoles) was dissolved in a mixture of water-methanol (30 ml, 1:1) containing 15% of formic acid and the solution was heated overnight at 80°. After addition of water (30 ml), the solution was extracted with chloroform and the extracts were washed with water and dried over magnesium sulfate. The solvent was removed and the resulting oil (0.657 g) was chromatographed on silica gel with dichloromethane-ether (9:1) as the eluent to give **6e** in 55% yield (0.356 g), mp 88-90° (ethanol-water) (lit [20] 89°); ir (potassium bromide): 1695 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 5.60 (s, 2H, CH_2), 7.3-7.55 (m, 5H, Ph), 8.05 (s, 1H, triazole H), 10.2 (s, 1H, CHO).

1-(*p*-Methoxyphenyl)-1,2,3-triazole-4-carbaldehyde (**6f**).

A solution of **3** (0.5 g, 2.9 mmoles) and 1.2 equivalents of *p*-methoxyaniline (0.43 g) in methanol (15 ml) was stirred overnight at room temperature. The precipitated **4f** was filtered off

and dried; yield 87% (0.7 g), mp 130° (ethanol).

Anal. Calcd. for $C_{16}H_{14}N_4O$ (mol wt 278): C, 69.05; H, 5.07. Found: C, 69.04; H, 5.01.

This compound (0.5 g, 1.8 mmoles) was heated in dimethyl sulfoxide (5 ml) at 80° for 1 day. The solution was poured into ice-water and the precipitate (0.45 g) was filtered off and dried. It consisted of a mixture of **4f** and **5f** which was not further separated.

This mixture (255 mg, 0.90 mmole) was dissolved in water-methanol (15 ml, 1:1) containing 10% of formic acid, and heated overnight at 80°. After cooling, water (15 ml) was added and the precipitate **6f** was filtered off and dried, yield 44% (80 mg), mp 154° (ethanol); ir (potassium bromide): 3140 (m, =CH), 1693 cm^{-1} (s, CO); ^1H nmr (dimethyl sulfoxide-d_6): δ 3.9 (s, 3H, OMe), 7.15 and 7.90 (two d, 4H, anisyl), 9.45 (s, 1H, triazole H), 10.1 (s, 1H, CHO).

Anal. Calcd. for $C_{10}H_9N_3O_2$ (mol wt 203): C, 59.11; H, 4.46. Found: C, 59.05; H, 4.53.

1-(*p*-Chlorophenyl)-1,2,3-triazole-4-carbaldehyde (**6g**).

A solution of ethyl propargylate (13 g, 0.13 mole) and *p*-chlorophenyl azide (20 g, 0.13 mole) in toluene (100 ml) was refluxed overnight. After cooling 1-(*p*-chlorophenyl)-4-ethoxycarbonyl-1,2,3-triazole precipitated in 83% yield (26 g), mp 169° (toluene). Note: the 1,5-isomer was also formed as minor component (*ca* 17%), but was not isolated.

To a solution of the 1,4-disubstituted triazole (5 g, 20 mmoles) in methanol (100 ml) was added in portions sodium borohydride (7.5 g). When hydrogen evolution ceased, the solution was heated for 2 hours. After cooling, water (100 ml) was added and the precipitated 1-(*p*-chlorophenyl-4-hydroxymethyl-1,2,3-triazole was filtered off, washed with water and dried, yield 91% (3.8 g), mp 141° (methanol).

This compound (2 g, 9.6 mmoles) and freshly prepared manganese dioxide (8.3 g, 96 mmoles) was stirred overnight in dichloromethane (100 ml) at room temperature. After filtration of the reaction mixture, the solvent was evaporated to give **6g** in 65% yield (1.3 g), mp 156° (chloroform-ether); ir (potassium bromide): 1710 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 7.5-7.8 (two d, 4 aromatic H), 8.52 (s, 1H, triazole H), 10.25 (s, 1H, CHO).

Anal. Calcd. for $C_9H_6ClN_3O$ (mol wt 207): C, 52.07; H, 2.91. Found: C, 52.13; H, 3.05.

Transformation of **6g** into **3**.

A solution of **6g** (0.7 g, 3.4 mmoles) and two equivalents of aniline (0.63 g) in methanol (15 ml) was stirred overnight at room temperature. The precipitate **5g** was collected in 73% yield (0.7 g), mp 145° (ethanol).

Anal. Calcd. for $C_{15}H_{11}ClN_4$ (mol wt 283): C, 63.72; H, 3.92. Found: C, 63.87; H, 3.98.

This compound (0.2 g, 0.7 mmole) was heated in dimethyl sulfoxide (2 ml) at 80° for 3 days. The solution was poured into ice-water and the precipitate was crystallized from ethanol to give **4g** in 56% yield (0.11 g), mp 155°.

Anal. Calcd. for $C_{15}H_{11}ClN_4$ (mol wt 283): C, 63.72; H, 3.92. Found: C, 63.63; H, 4.06.

Compound **4g** (0.2 g, 0.7 mmole) was dissolved in water-methanol (15 ml, 1:1) containing 10% of formic acid, and the whole was refluxed overnight. After addition of water (15 ml), the solution was extracted with chloroform and the combined extracts were washed with water and dried over magnesium sulfate. The solvent was removed and the residue was crystallized from chloroform-ether to give **3** in 73% yield (0.09 g), identical in all respects with an authentic sample.

1-(*p*-Nitrophenyl)-1,2,3-triazole-4-carbaldehyde (**6h**).

A solution of ethyl propargylate (4 g, 40 mmoles) and *p*-nitrophenyl azide (6.7 g, 40 mmoles) in toluene (100 ml) was refluxed overnight. After cooling, 1-(*p*-nitrophenyl)-4-ethoxycarbonyl-1,2,3-triazole precipitated in 71% yield (7.2 g), mp 185° (toluene). Note: The 1,5-isomer was also formed as minor component (ca 29%) and isolated by fractional crystallization of the filtrate, mp 100° (toluene).

To a solution of the 1,4-disubstituted triazole (1 g, 3.8 mmoles) in methanol (20 ml) was added in portions sodium borohydride (1.6 g). When hydrogen evolution ceased, the solution was heated for 1 hour. After cooling, water (20 ml) was added and the solution was concentrated. The precipitate (4-hydroxymethyl-1-nitrophenyl-1,2,3-triazole) was filtered off, washed with water and crystallized from methanol; yield 36% (0.3 g), mp 245°.

This compound (1 g, 4.5 mmoles) and freshly prepared manganese dioxide (4 g, 45 mmoles) was stirred overnight in dichloromethane (100 ml) at room temperature. After filtration of the reaction mixture, the solvent was evaporated and the residue crystallized from chloroform-ether to give **6h** in 47% yield (0.3 g), mp 168°; ir (potassium bromide): 1680 cm^{-1} (s, CO); ^1H nmr (dimethyl sulfoxide-d_6): δ 8.3 and 8.5 (two d, 4 aromatic H), 9.75 (s, 1H, triazole H), 10.2 (s, 1H, CHO).

Anal. Calcd. for $C_9H_6N_4O_3$ (mol wt 218): C, 49.55; H, 2.77. Found: C, 49.50; H, 2.85.

Transformation of **6h** into **3**.

A suspension of **6h** (0.39 g, 1.8 mmoles) and two equivalents of aniline (0.32 ml) in ethanol (30 ml) was stirred overnight at room temperature. The precipitate **5h** was filtered off in 51% yield (0.27 g), mp 180° (ethanol).

This compound (0.26 g, 0.89 mmole) was heated overnight in dimethyl sulfoxide (4 ml) at 80°. Then, the mixture was poured into water-methanol (50 ml, 1:1) containing 15% of formic acid and the whole was refluxed for 12 hours. The solution was poured into ice-water and extracted with chloroform. The extracts were washed with an aqueous solution of hydrochloric acid (1 *N*) and dried over magnesium sulfate. After evaporation of the solvent, **3** was obtained in 65% yield (0.1 g) and shown to be identical (ir, ^1H nmr) with an authentic sample.

1-Phenyl-1,2,3-triazole-4-carbaldehyde hydrazone (**4i**).

A solution of **3** (0.5 g, 2.9 mmoles) and 1.2 equivalents of hydrazine hydrate (0.17 g) in methanol (10 ml) was allowed to react at room temperature for 2 hours. The precipitate **4i** was filtered off and dried, yield 74% (0.4 g), mp 146° (chloroform); ir (potassium bromide): 3350 and 3180 cm^{-1} (NH_2); ^1H nmr (dimethyl sulfoxide-d_6): δ 7.14 (s, 1H, CH=N), 7.5-7.7 (two m, 3 aromatic H), 7.78 (br, 2H, NH_2), 7.9-8.0 (m, 2 aromatic H), 9.03 (s, 1H, triazole H).

Anal. Calcd. for $C_9H_9N_5$ (mol wt 187): C, 57.74; H, 4.84. Found: C, 57.75; H, 4.83.

1-Phenyl-1,2,3-triazole-4-carbaldehyde (*N*-Phenyl)hydrazone (**4j**).

A solution of **3** (0.3 g, 1.7 mmoles) and 1 equivalent of phenyl hydrazine (0.19 g) in methanol (15 ml) was stirred overnight at

room temperature. After removal of the solvent, the residue was crystallized from chloroform to give **4j** in 65% yield (0.29 g), mp 170° (chloroform); ir (potassium bromide): 3280 and 3140 cm^{-1} (NH_2); ^1H nmr (dimethyl sulfoxide-d_6): δ 6.85 (t, 1H, *p*-anilino H), 7.2-7.4 (s + m, 5H, CH=N + aromatic H), 7.5-7.7 (m, 3 aromatic H), 7.98 (d, 2 aromatic H), 9.16 (s, 1H, triazole H), 11.3 (s, 1H, NH).

Anal. Calcd. for $C_{15}H_{13}N_5$ (mol wt 263): C, 68.43; H, 4.98. Found: C, 68.30; H, 5.10.

4-Cyano-1-phenyl-1,2,3-triazole (**11**).

To a methanol solution (20 ml) of **3** (1 g, 5.8 mmoles) was added a neutralized aqueous solution of hydroxylamine hydrochloride (0.4 g, 5.8 mmoles in 4 ml) and the whole was stirred at room temperature for 1 day. After cooling, the precipitate **4k** was filtered off in 71% yield (0.78 g), mp 155° (ethanol).

Anal. Calcd. for $C_9H_8N_4O$ (mol wt 188): C, 57.44; H, 4.28. Found: 57.56; H, 4.13.

This compound (0.68 g, 3.62 mmoles) was dissolved in freshly distilled acetic anhydride (3.4 ml) and the solution was stirred at room temperature for 1 day. The precipitate **4m** was filtered off and dried, yield 60% (0.49 g), mp 144°.

Anal. Calcd. for $C_{11}H_{10}N_4O_2$ (mol wt 230): C, 57.39; H, 4.38. Found: C, 57.35; H, 4.27.

Compound **4m** (0.6 g, 2.6 mmoles) was heated in dimethyl sulfoxide (6 ml) at 90° for 50 hours. After cooling, the solution was poured into ice-water and the precipitate **11** was collected by filtration, yield 90% (0.4 g), mp 121° (chloroform-ether); ir (potassium bromide): 3140 (s, =CH), 2250 cm^{-1} (s, CN); ^1H nmr (deuteriochloroform): δ 7.5-7.9 (m, 5H, Ph), 8.5 (s, 1H, triazole H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 111.9 (CN), 120.4 (C-4), 130.5 (C-5), 120.9, 129.8, 129.9 and 135.5 (Ph). This compound was identical with an authentic sample obtained by dehydration of 1-phenyl-1,2,3,-triazole-4-carboxamide.

1-Phenyl-1,2,3-triazole-5-carbaldehyde (**7**).

This compound has been prepared as minor product from the cycloaddition of phenyl azide with propiolaldehyde diethyl acetal [10]. A more convenient procedure is as follows.

A solution of 4-methoxy-3-oxobutanoate (24.5 g, 168 mmoles), phenyl azide (20 g, 168 mmoles) and triethylamine (17 g, 168 mmoles) in methanol (250 ml) was refluxed for 10 days. The solvent was replaced by chloroform, washed with water and dried over magnesium sulfate. After concentration of the solution and addition of ether, 4-methoxycarbonyl-5-methoxymethyl-1-phenyl-1,2,3-triazole crystallized out in 24% yield (10.11 g), mp 115°.

This compound (10 g, 40 mmoles) was heated with sodium hydroxide (6.5 g, 160 mmoles) in methanol (100 ml) for 1 hour. The crystals which precipitated upon cooling, were dissolved in hot water and the solution was acidified with dilute hydrochloric acid (1*N*). The precipitate (8.4 g) was collected, dried and heated at the melting point (158°) until carbon dioxide evolution ceased. This furnished 5-methoxymethyl-1-phenyl-1,2,3-triazole in 90% yield, mp 52° (chloroform).

This compound (2 g, 10 mmoles), *N*-bromosuccinimide (1.9 g, 10 mmoles) and dibenzoyl peroxide (125 mg, 0.5 mmole) were heated overnight in carbon tetrachloride (150 ml). The warm mixture was filtered into water (300 ml) and the organic layer was washed three times with water and dried over magnesium sulfate. After removal of the solvent, **7** was obtained as an oil in 63% yield (1.1 g) and crystallized from petroleum ether, mp 77° (lit [10] 73°); ir (potassium bromide): 3125 (m, =CH), 1697 cm^{-1} (s, CO); ^1H nmr (deuteriochloroform): δ 7.6 (s, 5H, Ph), 8.4 (s, 1H, triazole H), 10.05 (s, 1H, CHO).

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