Heterocyclic Studies. 2 [1]. 5-Chloro-1*H*-1,2,3-triazole-4-carboxaldehydes, Preparation and Rearrangement Reactions

Preben H. Olesen, Flemming E. Nielsen, Erik B. Pedersen and Jan Becher*

Department of Chemistry, Odense University,
DK-5230 Odense M, Denmark

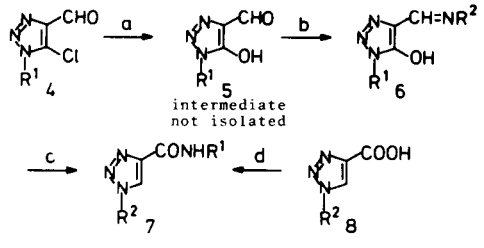
Received March 2, 1984

A general procedure for synthesis of 5-chloro-1*H*-1,2,3-triazole-4-carboxaldehydes **4** and the rearrangement reaction of 4-(*N*-substituted)iminomethylene-1*H*-1,2,3-triazol-5-ols **6** into *N*-substituted-1*H*-1,2,3-triazole-4-carboxamides **7** are described.

J. Heterocyclic Chem., **21**, 1603 (1984).

A great deal of interest has been focused on the triazoles [2]. When properly substituted, they can be useful starting materials for example for 8-azapurines and other condensed triazoles of biological interest [3]. This has inspired us to extend our work on heterocyclic β-chloroaldehydes in order to study the synthesis and potential applications of 5-chloro-1*H*-1,2,3-triazole-4-carboxaldehydes. Besides their synthesis, in this paper, we describe the hydrolysis of the chlorotriazole moiety and subsequent condensation reaction of the carboxaldehyde group with amines. The triazol-5-ol thus formed is shown to undergo a ring transformation reaction into 1,2,3-triazole-4-carboxamides by heating or by treatment with acetic acid.

5-Chloro-1*H*-1,2,3-triazole-4-carboxaldehydes

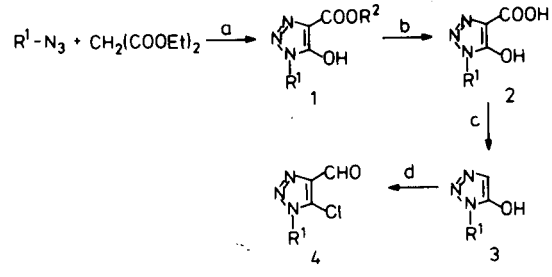


Compound	R^1	R^2
a	-benzyl	-Me
b	-*p*-chlorobenzyl	-Me
c	-*p*-methoxybenzyl	-Et
d	-phenyl	-Et

a: Sodium methoxide/methanol (**1a** and **1b**) [20] or sodium ethoxide/ethanol (**1c** and **1d**). b: Aqueous sodium hydroxide. c: Water. d: *N,N*-Dimethylformamide/phosphorus oxychloride.

The 5-chlorotriazole-4-carboxaldehydes **4** were obtained by the Vilsmeier-Haack reaction of triazol-5-ols **3** using phosphorus oxychloride and *N,N*-dimethylformamide. The reactions were finished after a short reaction time and the 1-benzyl derivatives of **4** were usually obtained in 60-94% yields (the 1-phenyltriazole **4d** was obtained in 35% yield). Although syntheses of the starting materials **1-3** were based on reported reaction procedures [4], most of the triazoles are new and yields of **1** were increased by the modified procedure. The subsequent chloroformylations have never been carried out in the triazole series before, and this reaction was found to be quite general here leading to the versatile new compounds **4**.

Ring Transformation into Triazole-4-carboxamides



Compound	R^1	R^2
a	benzyl	phenyl
b	benzyl	4-methoxyphenyl
c	benzyl	2-methylphenyl
d	benzyl	3-methoxyphenyl
e	4-chlorobenzyl	phenyl
f	4-chlorobenzyl	4-methoxyphenyl
g	4-chlorobenzyl	3-chloro-4-methylphenyl
h	4-chlorobenzyl	2-methoxy-5-methylphenyl
i	4-chlorobenzyl	4-chlorobenzyl
j	4-methoxybenzyl	phenyl

a: Aqueous potassium hydroxide. b: Primary amine/hydrochloric acid (4 *M*). c: Pyrolyses. d: Thionyl chloride/amine.

During work up of the carboxaldehydes **4**, we observed that they were readily hydrolysed to the corresponding 1,2,3-triazol-5-ols **5**. This hydrolysis took place after prolonged standing in aqueous acidic media, the hydrolysis

was followed by a ring opening reaction of the triazole ring. The ^{1}H nmr of the crude product showed this to be a mixture of two compounds, identified as a 5-hydroxy-1,2,3-triazole-4-carboxaldehyde (**5**) and a diazo compound showing strong ir absorption at 2140 cm^{-1}. Reaction of the crude reaction mixture with aniline resulted in a mixture of two products, **6a** and **7a** in the case of the 1-benzyl-1,2,3-triazole (**4a**). This mixture of **6a** and **7a** rearranged completely to compound **7a** on heating above the melting point.

5-Hydroxy-1,2,3-triazole-4-carboxylates **9** were first prepared by Dimroth [5] who demonstrated that such compounds will isomerize to amides of diazomalonic esters **10** when heated alone or dissolved in water or organic solvents.

Table 1

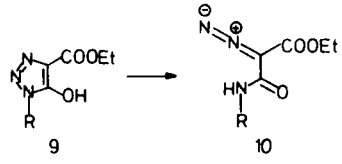
Starting Triazoles **1**, **2**, **3** and **4**

Compound No.	Yield %	Mp °C (Solvent)	Molecular formula	IR, ν cm^{-1} (potassium bromide)	^{1}H NMR (ppm)	Mass Spectra m/e (%)
1a	88 [a]	123 dec [b]		2800-2200, 2050-1800, 1720	3.83 (s, 3H, CH_3), 5.40 (s, 2H, CH_2), 7.3 (s, 5H, ArH), 11.67 (s, br, 1H, OH) in DMSO-d_6	233 (M^+, 25), 172 (13), 106 (20), 92 (17), 91 (100), 65 (16)
1b	91	115-116 (Ethanol)	$C_{11}H_{10}ClN_3O_3$ (267.67)	2700-2200, 2050-1850, 1715, 1600	3.80 (s, 3H, CH_3), 5.37 (s, 2H, CH_2), 7.15-7.55 (m, 4H, ArH), 9.10 (s br, 1H, OH), in DMSO-d_6	267 (M^+, 16), 209 (17), 206 (11), 142 (10), 140 (32), 127 (33), 126 (11), 125 (100), 91 (11), 89 (20), 69 (13)
1c	90	115-116 [c] (Ethanol)				277 (M^+, 7), 205 (14), 202 (10), 176 (25), 136 (18), 135 (15), 134 (11), 122 (10), 121 (100), 78 (11), 77 (14)
2a	91	88 dec [d]	$C_{10}H_9N_3O_3 \cdot H_2O$ (219.20)	3200-2700, 2700-2200, 2100-1800, 1705, 1610	5.35 (s, 2H, CH_2), 7.33 (s, 5H, ArH), 8.18 (s br, 4H, OH + COOH + H_2O) in DMSO-d_6	219 (M^+, 3), 91 (18), 44 (100)
2b	88	114 dec	$C_{10}H_8ClN_3O_3 \cdot H_2O$ (253.64)	3200-2700, 2700-2200, 2100-1800, 1705, 1605	5.33 (s, 2H, CH_2), 7.13-7.60 (m, 4H, ArH), 7.83 (s br, 4H, OH + COOH + H_2O) in DMSO-d_6	254 (MH^+, 1), 210 (19), 127 (31), 125 (100), 91 (12), 89 (13) [e]
2c	94	99-100 dec	$C_{11}H_{11}N_3O_3$ (249.22)	3200-2800, 2700-2200, 2100-1800, 1705, 1605	3.77 (s, 3H, CH_3), 5.30 (s, 2H, CH_2), 6.95 and 7.31 (2 d, 4H, J = 8 Hz, ArH), 10.93 (s br, 2H, OH and COOH) in DMSO-d_6	250 (MH^+, 1), 122 (10), 121 (100), 78 (10) [e]
3a	91 [f]	159-160 dec [g]		2800-2100, 1900-1650	5.32 (s, 2H, CH_2), 6.98 (s, 1H, triazole H), 7.33 (s, 5H, ArH), 8.8 (s br, 1H, OH) in deuteriochloroform + DMSO-d_6	175 (M^+, 0.5), 118 (13), 92 (11), 91 (100), 65 (12)
3b	92 [f]	159 dec (Ethanol)	$C_9H_9ClN_3O$ (209.63)	2700-2100, 1900-1650	5.32 (s, 2H, CH_2), 7.00 (s, 1H, triazole H), 7.13-7.53 (2 d, 4H, J = 8 Hz, ArH) in DMSO-d_6	209 (M^+, 1), 152 (14), 127 (32), 125 (100), 89 (13)
3c	88 [f]	160 dec (Ethanol)	$C_{10}H_{11}N_3O_3$ (205.21)	2700-2100, 1900-1650	3.76 (s, 3H, CH_3), 5.20 (s, 2H, CH_2), 6.83 and 7.25 (2 d, 4H, J = 8 Hz, ArH), 6.90 (s, 1H, triazole H) in deuteriochloroform + DMSO-d_6	205 (M^+, 2), 176 (12), 148 (10), 146 (10), 136 (10), 134 (18), 122 (11), 121 (100), 91 (20), 78 (19), 77 (28), 65 (11), 51 (20)
4a	90	36-37 (Ether/pentane)	$C_{10}H_8ClN_3O$ (221.64)	1705	5.57 (s, 2H, CH_2), 7.34 (s, 5H, ArH), 10.10 (s, 1H, CHO) in deuteriochloroform	221 (M^+, 4), 91 (100), 65 (13)
4b	76	76-77 (Ether)	$C_{10}H_7Cl_2N_3O$ (256.09)	1698, 1675 sh	5.57 (s, 2H, CH_2), 7.33 (s, 4H, ArH), 10.11 (s, 1H, CHO), in deuteriochloroform	255 (M^+, 3), 194 (12), 192 (37), 164 (14), 163 (17), 127 (34), 125 (100), 89 (15)
4c	64	58.5-59.5 (Ether)	$C_{11}H_{10}ClN_3O_2$ (251.67)	1695, 1611	3.83 (s, 3H, CH_3), 5.54 (s, 2H, CH_2), 6.93 and 7.37 (2 d, 4H, ArH), 10.17 (s, 1H, CHO) in deuteriochloroform	251 (M^+, 11), 188 (33), 159 (23), 121 (100), 78 (12), 77 (10)
4d	35	75-76 (Light petroleum 65-70°)	$C_9H_6ClN_3O$ (207.62)	1700, 1692	7.61 (s, 5H, ArH), 10.19 (s, 1H, CHO), in deuteriochloroform	207 (M^+, 0.6), 151 (12), 116 (10), 89 (14), 77 (100), 51 (36)

[a] Lit [4] 52% yield, no mp reported. [b] Lit [19] mp 119°. [c] Lit [16] 67% yield, mp 117°. [d] Lit [4] mp 90° dec. [e] From FAB-mass spectra. [f] Yield calculated from the ester. [g] Lit [4] 67% yield, mp 159° dec.

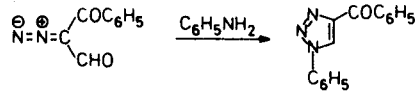
Table 1a

Compound No.	Analyses Found/Calcd. C	H	N	Cl
1b	49.74	3.77	15.68	13.11
	49.36	3.77	15.70	13.25
2a	50.92	4.84	18.04	
	50.63	4.67	17.71	
2b	44.48	3.75	15.37	13.28
	44.21	3.71	15.47	13.05
2c	52.87	4.64	16.51	
	53.01	4.45	16.86	
3b	51.67	3.88	20.01	16.89
	51.56	3.85	20.04	16.91
3c	58.65	5.45	20.51	
	58.53	5.40	20.48	
4a	54.05	3.63	18.64	16.07
	54.19	3.64	18.96	16.00
4b	46.59	2.73	16.26	27.47
	46.90	2.76	16.41	27.69
4c	52.39	4.01	16.60	14.09
	52.49	4.01	16.70	14.09
4d	52.13	2.91	20.12	
	52.06	2.91	20.24	



9 10

Stojanovic and Arnold [6] have later shown that formylbenzoyldiazomethane on reaction with aniline gives 1-phenyl-4-benzoyl-1,2,3-triazole.



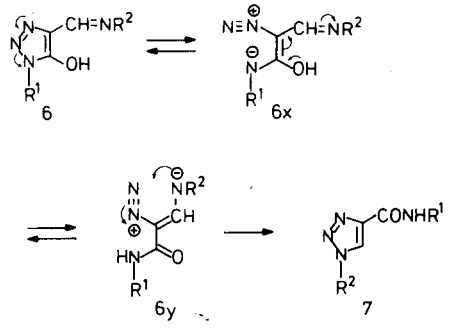
From these results it is reasonable to assume that the compound **6** formed by condensation of the 5-hydroxy-1,2,3-triazole-4-carboxaldehydes and anilines described here also isomerizes to **7**.

In order to avoid formation of a mixture of compounds after hydrolysis of the 5-chloro-1,2,3-triazole **4**, the reaction was carried out in aqueous alkaline medium. The resulting 5-hydroxy-1,2,3-triazole-4-carboxaldehydes **5** obtained were found however to be too unstable to be isolated. A primary amine was therefore added and the reaction mixture neutralized with dilute hydrochloric acid. A compound of type **6** was immediately precipitated (typically in 25-70% yields), demonstrating the stability of the 5-hydroxy-1,2,3-triazole-4-carboxaldehydes **4** towards ring opening in alkaline aqueous media. These results are in accordance with previously obtained results for the parent 1*H*-5-hydroxy-1,2,3-triazole-4-carboxaldehyde [7].

The compounds **6** isolated here were all isomerized to compounds of type **7**, upon heating to the melting point. This thermal isomerization of **6** into **7** took place in a remarkably clean and fast reaction. The reaction can readily be observed on a "Koffler hot stage", the coloured imino compounds **6** in most cases melt at lower temperatures than their isomers **7**, and almost immediately after melting they resolidify as colourless needles growing in the melt, these crystals then remelt at the melting point of the corresponding compounds of type **7**. The melting points given in Table 2 for the isomers **6** are therefore all approximate, and recorded on a "Koffler hot stage".

The isomerization of **6** into **7** can also be performed by reflux in glacial acetic acid, by the method described by Dimroth [8] and later by C. Pedersen [9] for the related rearrangement of 4-phenylazo-1,2,3-triazol-5-ols to 2-phenyltetrazole-5-carboxamides.

In order to confirm the structure of **7**, compounds **7a** and **7e** were prepared independently by another route, starting with the known 1-phenyl-1,2,3-triazole-4-carboxylic acid (**8**) [10]. *Via* the acid chloride this acid gave the expected *N*-substituted 1,2,3-triazole-4-carboxamide, which showed identical melting point and ir spectrum with the rearranged product obtained from **6**. A probable mechanism of the conversion **6** into **7** is depicted in the scheme.



The Dimroth like rearrangement described here must involve ring opening to the intermediate diazonium species **6x**. Rotation around the N-3-C-4 bond then takes place prior to the tautomerisation into **6y**. Recyclisation of the diazonium moiety to the imino nitrogen then gives the isomer **7**.

The ir spectra of compounds **6** show two strong bands between 1600 or 1700 cm^{-1}. No OH band is seen in the ir spectra due to intramolecular hydrogen bonding. Compounds **7** show bands typical of *N*-substituted amides, C=O, at 1650 cm^{-1} and a NH band at 3350 cm^{-1}.

The isomeric triazoles **6** and **7** are clearly differentiated by their ^1H nmr spectra. For compounds **6** the aliphatic benzylic protons are found as a singlet at 5.5 ppm. The iminomethylene proton is also seen in the spectra. The *N*-substituted-1,2,3-triazole-4-carboxamides **7** show a two proton doublet signal at 4.8 ppm with J = 4.5 Hz, assign-

Table 2

1-Substituted-4-(*N*-substituted)iminomethylene-5-hydroxy-1*H*-1,2,3-triazoles **6**

Compound No.	Yield %	Mp °C (solvent)	Molecular formula	^{1}H PMR (ppm) (trifluoroacetic acid)	IR ν cm^{-1} (potassium bromide)	Analyses % Found/Calcd. C	H	N	Mass Spectra m/e (%)
6a	61	177 (Ethanol)	$C_{16}H_{14}N_4O$ (278.32)	5.23 (s, 2H), 7.39 (s, 10H), 8.59 (s, 1H), 10.10 (s, 1H)	1672 1630	69.05 68.93	5.07 5.08	20.13 20.03	278 (M$^+$, 80) 91 (100)
6b	71	201 (Dioxane/ethanol)	$C_{17}H_{16}N_4O_2$ (308.44)	4.00 (s, 3H), 5.53 (s, 2H), 7.18 (d, 2H, J = 8.9 Hz), 7.42 (s, 5H), 7.67 (d, 2H, J = 9.2 Hz), 9.14 (s, 1H)	1670 1625	66.20 66.20	5.23 5.26	18.16 18.04	308 (M$^+$, 77) 91 (100)
6c	49	172 (Ethanol)	$C_{17}H_{16}N_4O$ (292.34)	2.37 (s, 3H), 5.17 (s, 2H), 7.25-7.86 (m, 4H), 7.33 (s, 5H), 9.23 (s, 1H)	1660 1632	69.85 69.85	5.52 5.49	19.16 19.04	292 (M$^+$, 53) 91 (100)
6e	51	173 (Ethanol)	$C_{16}H_{13}ClN_4O_2$ (312.50)	5.49 (s, 2H), 7.38 (s, 4H), 7.62 (s, 5H), 9.04 (s, 1H)	1675 1640	61.45 61.68	4.19 4.16	17.91 17.79	312 (M$^+$, 22) 125 (100)
6f	53	171 (EThanol)	$C_{17}H_{15}ClN_4O_2$ (342.50)	4.02 (s, 3H), 5.50 (s, 2H), 7.13-7.28 (d, 2H, J = 8.9 Hz), 7.39 (s, 4H), 7.60-7.75 (d, 2H, J = 9.2 Hz), 9.15 (s, 1H)	1670 1632	59.57 59.30	4.41 4.41	16.34 16.12	342 (M$^+$, 342) 125 (100)
6g	43	190 (Ethyl acetate)	$C_{17}H_{14}Cl_2N_4O$ (361.23)	2.52 (s, 3H), 5.53 (s, 2H), 7.30-8.70 (m, 3H), 7.41 (s, 4H), 9.23 (s, 1H)	1650 1622	56.53 56.63	3.91 3.93	15.51 15.51	360 (M$^+$, 74) 125 (100)
6h	35	234 (Ethyl acetate)	$C_{18}H_{17}ClN_4O_2$ (355.81)	2.42 (s, 3H), 4.08 (s, 3H), 5.54 (s, 2H), 7.00-7.20 (m, 7H), 9.27 (s, 1H)	1660 1625	60.71 60.59	4.82 4.76	15.75 15.58	356 (M$^+$, 100)
6i	32	230 (Ethyl acetate)	$C_{17}H_{14}Cl_2N_4O$ (361.23)	5.07 (s, 2H), 5.48 (s, 2H), 7.07 (s, 4H), 7.13 (s, 4H), 8.87 (broad, 1H)	1665 1630	56.28 65.53	3.85 3.91	15.48 15.51	360 (M$^+$, 25) 125 (100)
6j	25	165 (Ethanol)	$C_{17}H_{16}N_4O_2$ (308.26)	4.01 (s, 3H), 5.51 (s, 2H), 7.17 (d, 2H, J = 8.9 Hz), 7.42 (d, 2H, J = 9.2 Hz), 7.63 (s, 5H), 9.17 (s, 1H)	1660 1628	66.21 66.42	5.23 5.21	18.18 18.07	308 (M$^+$, 24) 121 (100)

ed to the aliphatic benzylic protons. The sharp one proton signal at 9.0 ppm in these spectra is assigned to the proton at C-5 in the triazole ring. The shift value for this proton is in agreement with the C-5 proton signals for similar compounds [11]. The NH proton in compounds **7** is found as a broad signal at 8.8 ppm.

The isomerization of **6** into **7** can easily be followed by ^{1}H nmr spectroscopy, and takes place over a period of 3 to 4 weeks in trifluoroacetic acid at room temperature. The singlet at 5.5 ppm disappears, while a doublet at 4.8 ppm develops. The mass spectra does not distinguish between the isomers **6** and **7**, as both types of compounds give the same fragmentation pattern due to primary loss of nitrogen.

As seen in the table we have found that this rearrangement takes place with a number of different *N*-substituents. Changing of the 4-substituents in the 1-benzylic group did not affect the rearrangement, nor did the substitution pattern in the amine part of **6** as well as change of the electron releasing or withdrawing effects of these substituents. It can therefore be concluded that this rearrangement is quite general for the 4-(*N*-substituted)iminomethylene-5-hydroxy-1*H*-1,2,3-triazoles **6**.

EXPERIMENTAL

Microanalyses were carried out at NOVO A/S Bagsvaerd by Mr. Rolf Amsler. The instrumentation is the following: ^{1}H nmr, Jeol JNM-PMX 60; ir, Perkin Elmer 580; ms: Varian MAT CH7A; mp, Büchi apparatus (uncorrected).

5-Hydroxy-1-(phenylmethyl)-1*H*-1,2,3-triazole-4-carboxylic Acid Methyl Ester (**1a**).

The method is modified from a procedure previously described by Gompper [4]. To a solution of sodium methoxide [19.8 g (0.86 mole) of sodium in 500 ml of methanol] was added 136.1 g (0.85 mole) of diethyl malonate [20] in one portion. To this solution was added 113.2 g (0.85 mole) of benzyl azide [12,13] during 15 minutes at room temperature. The reaction mixture was then heated under reflux for 15 hours. The solution was cooled to room temperature and the solvent was removed *in vacuo* to give a syrup. This was dissolved in 400 ml water and acidified to *p*H 1-2 with hydrochloric acid (4 *M*). After stirring in an ice-bath for one hour the resulting precipitate was filtered off and washed with water and diethyl ether to give 174.2 g (88%) of the title compound **1a**.

1-[(4-Chlorophenyl)methyl]-5-hydroxy-1*H*-1,2,3-triazole-4-carboxylic Acid Methyl Ester (**1b**).

Compound **1b** was prepared in a yield of 236.5 g (91%) from diethyl malonate (160.2 g, 1.0 mole) [20] and *p*-chlorobenzyl azide [14,15] (162.6 g, 0.97 mole) in a sodium methoxide solution [23.0 g (1.0 mole) of sodium in 500 ml of methanol] as described above for **1a**.

5-Hydroxy-1-[(4-methoxyphenyl)methyl]-1*H*-1,2,3-triazole-4-carboxylic Acid Ethyl Ester (**1c**).

Table 3

1-Substituted-*N*-substituted-1*H*-1,2,3-triazole-4-carboxamides **7**

Compound No.	Yield %	Mp °C (solvent)	Molecular formula	^{1}H NMR (ppm) (trifluoroacetic acid)	IR ν cm^{-1} (potassium bromide)	Analyses % Found/Calcd. C	H	N	Mass Spectra m/e (%)
7a	85	203-204 (Acetone)	$C_{16}H_{14}N_4O$ (278.32)	4.82 (d, 2H, J = 4.5 Hz), 7.37 (s, 5H), 7.72 (s, 5H), 8.77 (broad, 1H), 9.09 (s, 1H)	1655 3360	69.05 68.92	5.07 5.06	20.13 20.08	278 (M$^+$, 88) 91 (100)
7b	83 (80)	230-231 (Ethyl acetate)	$C_{17}H_{16}N_4O_2$ (308.44)	4.03 (s, 3H), 4.86 (d, 2H, J = 4.5 Hz), 7.23 (d, 2H, J = 9.0 Hz), 7.40 (s, 5H), 7.79 (d, 2H, J = 8.5 Hz), 8.83 (broad, 1H), 9.13 (s, 1H)	1690 3440	66.20 66.03	5.23 5.26	18.16 18.00	308 (M$^+$, 55) 91 (100)
7c	70 (53)	177-178 (Ethyl acetate)	$C_{17}H_{16}N_4O$ (292.34)	2.26 (s, 3H), 4.84 (d, 2H, J 4.5 Hz), 7.30-7.60 (m, 4H), 7.33 (s, 5H), 8.83 (s, 1H), 8.83 (broad, 1H)	1650 3300	69.85 70.04	5.52 5.48	19.16 19.08	292 (M$^+$, 70) 91 (100)
7d	35 [a]	180-181 (Ethanol)	$C_{17}H_{16}N_4O_2$ (308.44)	4.01 (s, 3H), 4.74 (d, 2H, J = 4.5 Hz), 7.1-7.6 (m, 9H), 8.73 (broad, 1H), 9.07 (s, 1H)	1650 3310	66.20 66.34	5.23 5.21	18.16 18.08	308 (M$^+$, 100)
7e	80	217-218 (Ethyl acetate)	$C_{17}H_{13}ClN_4O_2$ (312.50)	4.83 (d, 2H, J = 4.5 Hz), 7.34 (s, 5H), 7.73 (s, 4H), 8.96 (broad, 1H), 9.12 (s, 1H)	1657 3320	61.45 61.23	4.19 4.15	17.91 17.56	312 (M$^+$, 52) 144 (100)
7f	87	214-215 (Ethyl acetate)	$C_{17}H_{15}ClN_4O_2$ (342.50)	4.07 (s, 3H), 4.83 (d, 2H, J = 4.5 Hz), 7.31 (d, 2H, J = 9.0 Hz), 7.36 (s, 5H), 7.83 (d, 2H, J = 8.5 Hz), 8.96 (broad, 1H), 9.07 (s, 1H)	1655 3335	59.57 59.58	4.41 4.41	16.34 16.27	342 (M$^+$, 18) 125 (100)
7g	84 (75)	220-221 (Ethyl acetate)	$C_{17}H_{14}Cl_2N_4O$ (361.23)	2.50 (s, 3H), 4.72 (d, 2H, J = 4.5 Hz), 7.33 (s, 4H), 7.3-7.8 (m, 3H), 8.99 (broad, 1H), 8.99 (s, 1H)	1650 3310	56.53 56.65	3.91 3.86	15.51 15.40	360 (M$^+$, 59) 125 (100)
7h	90	171-172 (Ethanol)	$C_{18}H_{17}ClN_4O_2$ (355.82)	2.43 (s, 3H), 3.97 (s, 3H), 4.72 (d, 2H, J = 4.5 Hz), 7.2-7.6 (m, 3H), 7.33 (s, 4H), 8.74 (broad, 1H), 9.20 (s, 1H)	1662 3298	60.41 60.71	4.73 4.82	15.56 15.75	356 (M$^+$, 100)
7i	90	207-208 (Ethyl acetate)	$C_{17}H_{14}Cl_2N_4O$ (361.23)	4.77 (d, 2H, J = 4.5 Hz), 5.80 (s, 2H), 7.33 (s, 4H) 6.43 (s, 4H), 8.70 (s, 1H), 8.70 (broad, 1H)	1640 3290	56.26 56.53	3.86 3.91	15.52 15.51	360 (M$^+$, 38) 140 (100)
7j	84	195-196 (Ethanol)	$C_{17}H_{16}N_4O_2$ (308.26)	4.04 (s, 3H), 4.77 (d, 2H, J = 4.5 Hz), 7.10 (d, 2H), 7.45 (d, 2H), 7.75 (s, 5H), 8.72 (broad, 1H), 9.12 (s, 1H)	1650 3295	65.90 66.21	5.19 5.23	18.03 18.18	308 (M$^+$, 80) 136 (100)

[a] Yield calculated from the aldehyde. Yields given in brackets refer to preparation by method B.

Compound **1c** was prepared by the method described previously [16] but the smaller amount of solvent used here increased the yield substantially. Thus reaction of 63.6 g (0.39 mole) of *p*-methoxybenzyl azide [16] and 62.5 g (0.39 mole) of diethyl malonate in a solution of sodium ethoxide [9.0 g (0.39 mole) of sodium in 250 ml of ethanol] gave 96.8 g (90%) of the pure title compound **1c**.

1-Substituted-5-hydroxy-1*H*-1,2,3-triazole-4-carboxylic Acids, **2a-c**.

These compounds were prepared by saponification of the esters **1a-c** by the method reported for **2a** [4], except that **1c** was boiled in the aqueous sodium hydroxide for one hour. Analytically pure material was obtained by dissolving the product in sodium hydroxide (2 *M*) followed by addition of cold hydrochloric acid (4 *M*). The precipitate was washed with water and dried *in vacuo*.

1-Substituted-1*H*-1,2,3-triazol-5-ols **3a-c**.

These compounds were prepared by decarboxylation of crude **2a-c** according to the known procedure for the preparation of **3a** [4].

1-Phenyl-1*H*-1,2,3-triazol-5-ol (**3d**).

This compound was prepared according to Dimroth [17] by saponification and decarboxylation of 5-hydroxy-1-phenyl-1*H*-1,2,3-triazole-4-carboxylic acid, ethyl ester (**1d**) [18].

5-Chloro-1*H*-1,2,3-triazole-4-carboxaldehydes **4a-d**. General Procedure.

Phosphorus oxychloride (196 ml, 2.1 moles) was added dropwise to ice cold *N,N*-dimethylformamide (70 ml, 0.9 mole) in a three neck flask equipped with a dropping funnel, mechanical stirrer, thermometer and a reflux condenser with drying tube. The temperature was kept below 5°.

To the Vilsmeier-Haack reagent was added the required 5-hydroxy-1*H*-1,2,3-triazole **3a-d**, (0.3 mole) in one portion whereupon the mixture was refluxed for 15 minutes. The resulting clear solution was allowed to cool to room temperature and added to 2 ℓ of ice-water followed by further cooling for 15-60 minutes. The chloroformyl compounds **4a** and **4d** were isolated from the water phase by extraction with ether (500 ml and 4 × 250 ml). The combined extracts were washed successively with water (200 ml), saturated aqueous sodium hydrogen carbonate (200 ml) and water (200 ml), dried over sodium sulphate and evaporated to dryness *in vacuo*.

The chloroformyl compounds which precipitated (**4b** and **4c**) were isolated by filtration and washed with water (200 ml), saturated aqueous sodium hydrogen carbonate (200 ml) and water (2 × 200 ml). An additional amount of **4c** was further obtained by extraction of the aqueous filtrate with ether (4 × 250 ml) as described above for **4a** and **4d**.

4-(*N*-Substituted)iminomethylene-5-hydroxy-1*H*-1,2,3-triazoles, **6**. General Procedure.

The required 5-chlorotriazole-4-carboxaldehyde (**4**) (7.5 mmoles) was added to a solution of potassium hydroxide (2.1 g) in water/ethanol 1:1 (30 ml). The reaction mixture was heated at 60° for 3 hours, and then allowed to cool to room temperature. The amine (7.5 mmoles) was now added, and the mixture neutralised with hydrochloric acid (4 *M*), and allowed to stand with stirring for one hour. The precipitated crystals were filtered, dried and recrystallised according to Table 2.

N-Substituted-1*H*-1,2,3-triazole-4-carboxamides, **7**. Method A. General Procedure.

Compound **6** (0.5 g) was heated to the melting point and kept at this temperature for 2 minutes. The isomerised product crystallised upon cooling and was recrystallised according to Table 3.

Method B. Compounds **7b**, **7c** and **7g**.

Compound **6** (0.2 g) was heated with reflux in acetic acid (10 ml) for 3 hours. After cooling 15 ml water was added. The precipitated crystals were filtered, dried and recrystallised according to Table 3.

Preparation of Authentic *N*-Substituted-1*H*-1,2,3-triazole-4-carboxamides, **7a** and **7e**.

1-Phenyl-1,2,3-triazole-4-carboxylic acid (**8**) (0.4 g) was mixed with thionyl chloride (5 ml) and heated with reflux for one hour. Excess thionyl chloride was removed *in vacuo*, whereupon the crude acyl chloride was dissolved in dry toluene (20 ml) and benzylamine (0.5 ml) was added with cooling. The precipitated crystals of **7a** or **7e** were filtered and recrystallised.

1-Phenyl-*N*-(phenylmethyl)-1*H*-1,2,3-triazole-4-carboxamide.

This compound was obtained in 68% yield mp 203-204° (acetone) and was found to be identical with compound **7a**.

1-Phenyl-*N*-[(4-chlorophenyl)methyl]-1*H*-1,2,3-triazole-4-carboxamide.

This compound was obtained in 76% yield, mp 217-218° (ethyl acetate) and was found to be identical with compound **7e**.

REFERENCES AND NOTES

[1] J. Becher and P. H. Olesen, Heterocyclic Studies, 1, to be published.

[2a] T. L. Gilchrist and G. E. Gymer in "Advances in Heterocyclic Chemistry", Vol 16, A. R. Katritzky and A. J. Boulton, eds, Academic Press, 1974, p 33; [b] K. T. Finley in "Triazoles: 1,2,3", J. A. Montgomery, Volume ed, in "The Chemistry of Heterocyclic Compounds", A. Weisberger and E. C. Taylor, eds, John Wiley and Sons, 1980.

[3a] Y. Mizuno, T. Itoh and A. Nomura, *Heterocycles*, **17**, 615 (1982); [b] S.-F. Chen, R. P. Panzica, D. L. Dexter, M.-Y. W. Chu and P. Calabresi, *J. Heterocyclic Chem.*, **19**, 285 (1982); [c] G. Jones and R. Sliskovic in "Advances in Heterocyclic Chemistry", Vol 34, A. R. Katritzky, ed, Academic Press, 1983, p 79.

[4] R. Gompper, *Chem. Ber.*, **90**, 382 (1957).

[5] O. Dimroth, *Ann. Chem.*, **399**, 91 (1913).

[6] F. M. Stojanovic and Z. Arnold, *Collect. Czech. Chem. Commun.*, **32**, 2155 (1967).

[7] S. Romani, G. Virleitner and W. Klötzer, *Ann. Chem.*, 1518 (1979).

[8] O. Dimroth, *Ann. Chem.*, **335**, 1 (1904).

[9] C. Pedersen, *Acta Chem. Scand.*, **12**, 1236 (1958).

[10] R. Huisgen, R. Knorr, L. Möbius and G. Szemies, *Chem. Ber.*, **98**, 4014 (1965).

[11] G. B. Barlin and T. J. Batterham, *J. Chem. Soc. B*, 516 (1967).

[12] R. H. Wiley, K. F. Hussing and J. Moffat, *J. Org. Chem.*, **21**, 190 (1956).

[13] T. Curtius and G. Ehrhart, *Chem. Ber.*, **55**, 1559 (1922).

[14] H. Hayashi, A. Ohno and S. Oka, *Bull. Inst. Chem. Res., Kyoto Univ.*, **53**, 489 (1975); *Chem. Abstr.*, **85**, 76937m (1976).

[15] A. J. Hubert, *Bull. Soc. Chim. Belg.*, **79**, 195 (1970).

[16] D. R. Buckle and C. J. Rockell, *J. Chem. Soc., Perkin Trans. I*, 627 (1982).

[17] O. Dimroth, *Ber.*, **35**, 4041 (1902).

[18] P. K. Dutt, *J. Chem. Soc.*, **123**, 265 (1923).

[19] O. Dimroth, *Ann. Chem.*, **373**, 365 (1910).

[20] The diethyl malonate was used here as starting material, but due to the large amount of methanol used as solvent, transesterification to the methyl ester took place during the reaction, resulting in isolation of the pure methyl ester.