Replacement of Aryl by Alkyl in 1-Substituted 1*H*-1,2,3-Triazole-4-carbaldehydes

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1-Phenyl-1,2,3-triazole-4-carbaldehyde is readily transformed into 1-alkyl-1,2,3-triazole-4-carbaldehydes by thermal isomerization of the corresponding imines, followed by acid hydrolysis.

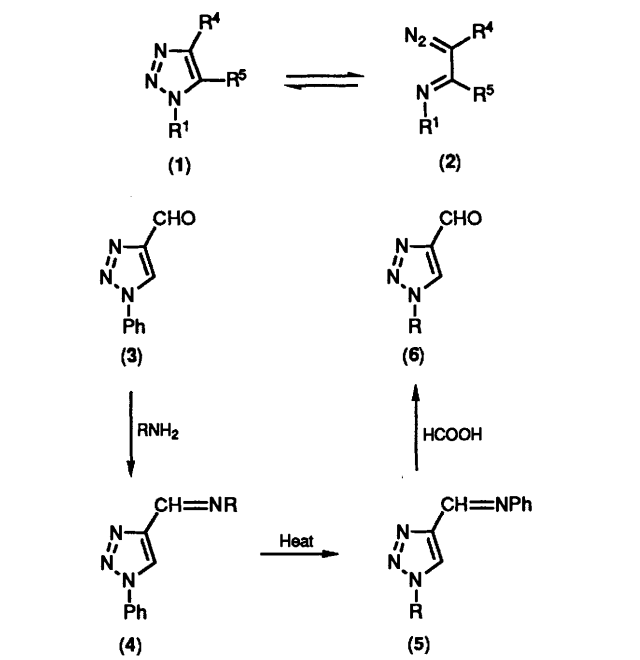
1*H*-1,2,3-Triazoles (**1**) are able to equilibrate with diazoimines (**2**) and the equilibrium position depends primarily on the nature of the substituents.[1] Thus, strong electron-withdrawing N-1 substituents (*e.g.* CN, RSO_2) stabilize the open-chain diazoimine (**2**), whereas alkyl and aryl substituents shift the equilibrium towards the triazole form (**1**).

The mechanism of the classical Dimroth rearrangement of 5-amino-1-aryltriazoles into 5-anilinotriazoles is based on this equilibrium,[2] and several other triazole rearrangements have been discovered recently which all involve diazoimines as intermediates. These are the thermal rearrangements of 5-hydrazinotriazoles,[3] 5-azidotriazoles,[4] 5-(diazomethyl)triazoles,[5] and 4-(iminomethyl)triazoles.[6] Since aldehydes and their Schiff bases are interconvertible, we have now devised a sequence to transform 1-phenyl-1,2,3-triazole-4-carbaldehyde (**3**) into 1-alkyl-1,2,3-triazole-4-carbaldehydes (**6**) according to the Scheme.

The 4-(iminomethyl)triazoles (**4a–e**), derived from 1-phenyl-1,2,3-triazole-4-carbaldehyde (**3**)[7] and alkylamines, were found to rearrange smoothly and completely into the isomeric triazoles (**5a–e**) when heated in DMSO solution at 80 °C for 16 h. They were hydrolysed with 10–15% of formic acid in boiling water–methanol (1:1) to furnish (**6a–e**) (Table).* The yields recorded in the Table are not optimized since all steps are virtually quantitative according to NMR measurements, and loss of product is due to the isolation and purification procedures (extraction, crystallization, chromatography). The isomerization of (**4**) into (**5**) represents the first examples of triazole rearrangements with a hydrogen atom at the 5-position.

The alternative method for the synthesis of (**6**) would involve a 1,3-dipolar cycloaddition of alkyl azides with acetylenes (propiolaldehyde, ethyl propiolic ester or prop-2-ynyl alcohol). Our method offers the advantage of using the safe phenyl azide instead of the low-boiling explosive alkyl azides,[8] necessary for the preparation of the lower alkyl derivatives, *e.g.* (**6a, b**). Furthermore, it allows the synthesis of sterically hindered derivatives, *e.g.* (**6d**), which would be difficult to obtain by the classical method.

In conclusion, 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 synthesis of 1-alkyl-1,2,3-triazole-4-carbaldehydes.



	a	b	c	d	e
R	Me	Et	Pr^i	Bu^t	$PhCH_2$

Scheme.

* All compounds are unambigously characterized by IR, ^1H and ^{13}C NMR, and mass spectral data.

Table. Yields (%) and m.p. (°C in parentheses)[a]

Compound	(4)	(5)	(6)
a	74 (87)	95 (154)	67 (113)
b	52 (35)	84 (83)	48 (oil)
c	74 (oil)	[b]	34 (oil)
d	95 (oil)	75 (105)	52 (oil)
e	84 (111)	90 (120)	55 (88)

[a] The products were recrystallized as follows: (**4a**) and (**5a**) in ether–light petroleum, (**4b**) in light petroleum, (**4e**), (**5b**), and (**5d**) in ethanol, (**5e**) in ethyl acetate, (**6a**) in chloroform–ether, and (**6e**) in ethanol–water.
[b] This compound was not further purified, but directly converted into (**6c**).

Experimental

Typical Procedure: 1-*Methyl*-1,2,3-*triazole*-4-*carbaldehyde* (**6a**).—To a solution of (**3**) (1 g, 5.8 mmol) in methanol (20 ml) was added an aqueous solution (40%) of methylamine (1 ml, 2 equiv.), and the whole was stirred overnight at room temperature. The solvent was removed under reduced pressure and the resulting oil was dissolved in chloroform, washed with water, and dried ($MgSO_4$). The solvent was evaporated to give (**4a**) (0.8 g, 74%), m.p. 87 °C (ether–light petroleum). This compound (0.42 g, 2.2 mmol) was heated overnight in DMSO (4 ml) at 80 °C. 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 ($MgSO_4$) and evaporated to give a further crop of (**5a**) (0.2 g), m.p. 154 °C (ether–light petroleum). Compound (**5a**) (0.2 g, 1.1 mmol) was dissolved in a mixture of water–methanol (1:1; 15 ml) containing 15% of formic acid and the solution was heated overnight at 80 °C. After cooling, the reaction mixture was poured into water and extracted with chloroform; the water layer was neutralized with $NaHCO_3$ and then extracted with dichloromethane. These extracts were dried ($MgSO_4$) and evaporated to give (**6a**) (0.08 g, 67%), m.p. 113 °C (chloroform–ether), (lit.,[9] 113 °C).

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