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1,2,3-Triazol-1-imines. Part 3: Tandem 1,3 cycloaddition–rearrangement and open chain reactions of 2-aryl-*N*-aroyl-4,5-dimethyl-1,2,3-triazol-1-imines with dimethyl acetylenedicarboxylate†

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Abstract

The tandem 1,3 cycloaddition–rearrangement and open chain reactions of 2-aryl-*N*-aroyl-4,5-dimethyl-1,2,3-triazol-1-imines with DMAD at room temperature and in refluxing toluene are described.

Keywords: 1,2,3-triazol-1-imines; aromatic azomethine imines; 1,3-dipolar cycloaddition.

Heteroaromatic *N*-imines constitute a highly useful class of compounds, especially as synthetic intermediates in preparative heterocyclic chemistry.[1] Their synthetic utility and reactivity has been thoroughly investigated over the last decades. Of particular interest is their ability to function as 1,3-dipoles in cycloaddition reactions, which was first demonstrated by Huisgen[2] and co-workers some time ago, giving rise to many interesting heterocyclic systems.[3] The reactivity stems from the azomethine imine structure of the *N*-imines. The azomethine imine moiety is incorporated into a heteroaromatic ring system. At present, several research groups still continue to contribute in the field.[4]

Recently, we have developed an efficient way of synthesizing the title compounds by oxidation of biacetyl aroyl-arylhydrazones[5] and measured their electric dipole moments.[6] In continuation of our work in the field, herein we wish to report the 1,3-dipolar cycloaddition and open chain reactions of 1,2,3-triazol-1-imines **1** with dimethyl acetylenedicarboxylate (DMAD).

When the title 1,2,3-triazol-1-imines **1** were heated at reflux in toluene with DMAD as dipolarophile,[7] good yields of the substituted dihydro-1,2,3-triazines **3** were obtained (Scheme 1

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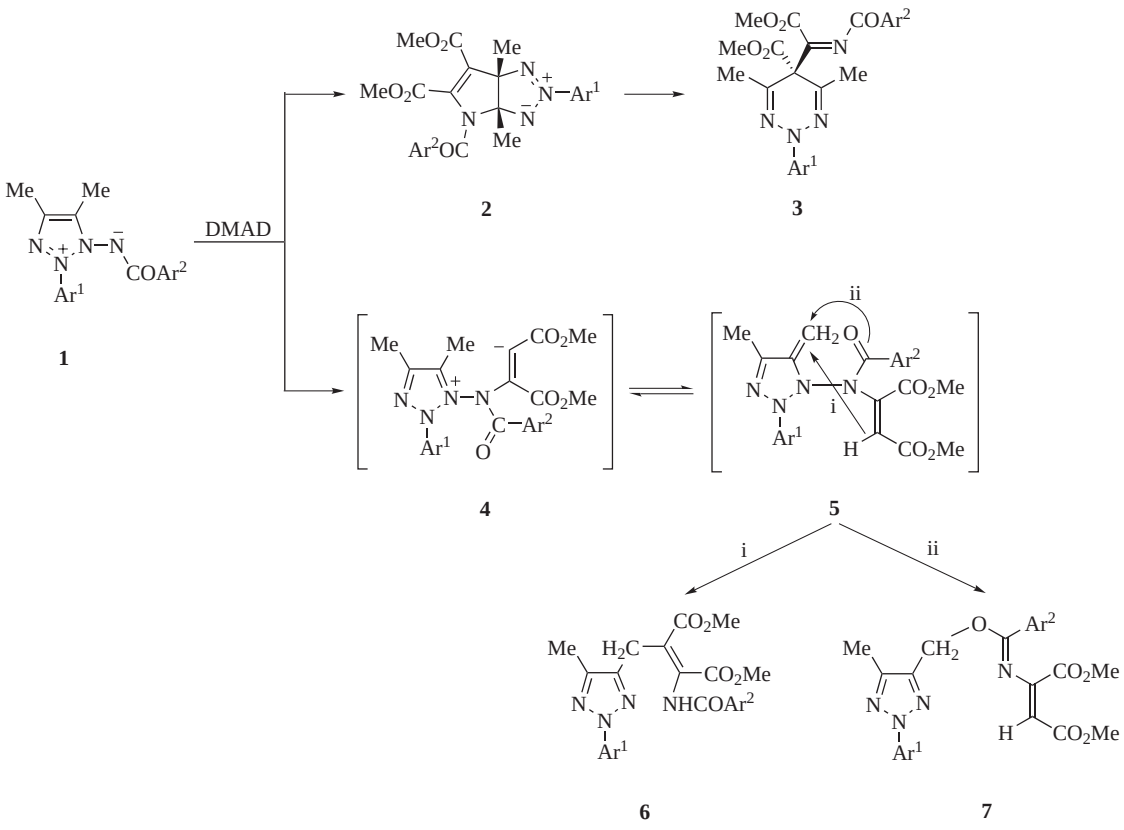

a Ar^1= Ph, Ar^2= Ph
b Ar^1= *p*-MePh, Ar^2= Ph
c Ar^1= *p*-ClPh, Ar^2= Ph
d Ar^1= *p*-NO_2Ph, Ar^2= Ph
e Ar^1= Ph, Ar^2= *p*-NO_2Ph

Scheme 1. Cycloaddition and open chain reaction sequence

and Table 1). In two cases (entries 2 and 5, Table 1) the substituted pyrrolo[2,3-*d*]-1,2,3-triazoles **2b** and **2e** were also isolated from the reaction mixture in low yields. Compounds **2** are considered to be formed by the same reaction route leading to compounds **3**. In addition, almost in all cases, compounds **6**, which result from the open chain reaction sequence depicted in Scheme 1 (vide infra), were also obtained.

In order to define the scope and the limitations of the title reaction, we also performed the cycloaddition experiments at room temperature and discovered that temperature exerts an interesting influence on product formation. In particular, on going from refluxing toluene to room temperature,[7] the yield of dihydro-triazine **3** was minimized or nullified while the yield of pyrrolo-triazole **2** was increased (Table 1). At the same time, the yield of product **6** was also increased and a new product appeared, to which structure **7** was ascribed (Scheme 1).

The above results can be explained in terms of two concurrent reaction pathways. The first involves a cycloaddition reaction in which the initially formed unstable cycloadduct leads, via a stepwise rearrangement, to the pyrrolo-1,2,3-triazole **2** (Scheme 1). Further rearrangement leads finally to the dihydro-1,2,3-triazine **3**. This multistep mechanism was first proposed by Butler

Table 1
Isolated yields of products derived from 1,2,3-triazol-1-imines **1** and DMAD at room temperature and in refluxing toluene

Entry	Starting imine **1**	Isolated Yields (%)									
		2		**3**		**6**		**7**		Total	
		Δ^a	Rt	Δ^a	Rt	Δ^a	Rt	Δ^a	Rt	Δ^a	Rt
1	**1a**	–	33	68	5	7	20	–	12	75	70
2	**1b**	8	36	74	5	6	16	–	9	88	66
3	**1c**	–	5	80	12	5	58	–	6	85	81
4	**1d**	–	14	23	–	18	21	–	6	41	41
5	**1e**	5	6	45	12	–	5	–	5	50	28

[a] Refluxing toluene.

and co-workers in order to explain the products of the reaction of 1,2,3-triazole-*N*-oxides with dialkyl acetylenedicarboxylates.[8] Similar mechanisms were also found to operate in a series of cycloaddition reactions of 1,2,3-triazol-imines with various dipolarophiles.[9]

On the other hand, formation of products **6** and **7** can be rationalized by an open chain reaction sequence, operating concurrently to the cycloaddition pathway and which probably involves the tautomeric form **5** of the intermediate **4** (Scheme 1). Finally, products **6** and **7** result from an intramolecular attack on the exocyclic methylene group in **5** by carbon or oxygen, respectively, which is followed by N–N bond cleavage. It should be noticed that the total yields of the open chain products **6** and **7** are comparable to those of the cycloaddition products **2** and **3** when the reaction is carried out at room temperature, while at higher temperature the total yields of the cycloaddition products are overwhelming (Table 1).

The product dichotomy due to temperature variation is unprecedented to our knowledge in the cycloaddition chemistry of the heterocyclic *N*-imines and apparently originates from the relatively higher energy demands of the cycloaddition reaction, compared to the open chain reaction. However, the latter is only sluggish at room temperature and also inefficient at higher temperature apparently because the generation of the assumed intermediate **5** cannot favorably compete with the cycloaddition.

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7. Typical experimental conditions. *Cycloaddition reactions of 1,2,3-triazol-1-imines* ***1*** *with DMAD in refluxing toluene*: A solution of **1** (1 mmol) and DMAD (3 mmol) in dry toluene (5 mL) was refluxed until TLC analysis showed almost complete consumption of the starting material (2–9 h). The solvent was removed in vacuo and the residue was chromatographed on a silica gel low-pressure column using as eluent mixtures of petroleum ether–ethyl acetate of gradually increasing polarity. *Cycloaddition reactions of* ***1*** *with DMAD at room temperature*: The same as the above procedure was followed for the room temperature experiments. Reaction times were generally longer (4–42 days). All compounds were identified by the usual spectroscopic techniques, especially by their ^{1}H and ^{13}C NMR spectra, which showed all of the expected signals. All of the compounds gave satisfactory microanalyses. X-Ray crystal structures were determined for compounds **3a** and **7b**.
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