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2-Diazoacethydrazide derivatives and their ring-chain transformations

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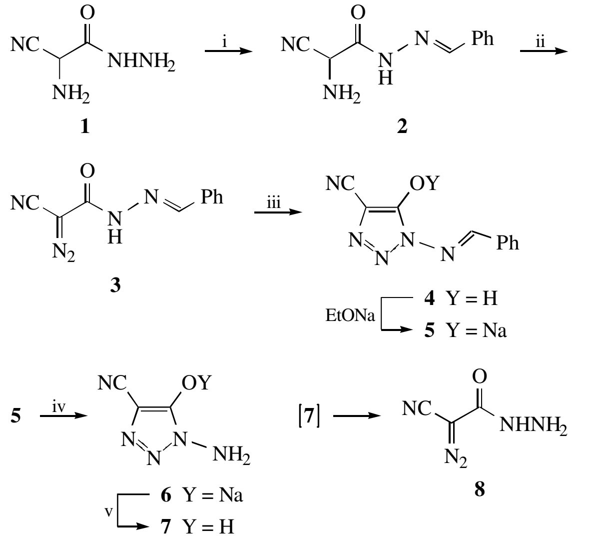
1-Amino-1,2,3-triazol-5-olates 6, 13 and 14 have been obtained by the introduction of a diazo group into *N*-benzylidene-protected hydrazides of cyanoacetic and malonic acids. These compounds form open-chain isomers of 1-amino-5-hydroxy-1,2,3-triazoles upon acidification with an aqueous solution of HCl. Compounds 8, 15 and 16 are the first examples of the group of -diazoacethydrazides.

-Diazoacetamides and the products of their cyclisation, 5-hydroxy-1,2,3-triazoles, have been extensively studied,[1,2] though until this report, the relevant literature has carried no examples of diazo compounds containing the hydrazide group in the -position. This paper presents data on the synthesis of the first examples of 2-diazoacethydrazides and derivatives of their cyclic isomers, 1-amino-1,2,3-triazoles.

We showed previously[3] that the interaction of 2-amino-2-cyanoacethydrazide **1** with sodium nitrite in an aqueous solution of hydrochloric acid (or with alkyl nitrites in glacial acetic acid) proceeds simultaneously at the amino and hydrazide groups with the formation of 2-diazo-2-cyanoacetazide. To carry out the reaction selectively at the amino group, we protected of the hydrazide group with *N*-benzylidene.



Scheme 1 *Reagents and conditions*: i, PhCHO, EtOH, 20 °C; ii, Bu^{t}ONO, AcOH, 10 °C; iii, 20 °C, 24 h in DMSO or $CHCl_3$; iv, H_2NNH_2, EtOH, 78 °C, 12 h; v, HCl, H_2O, 0–1 0 °C.

Interaction of hydrazide **1** with benzaldehyde leads to smooth formation of hydrazone **2**. Reaction of **2** with butyl nitrite in glacial acetic acid yields *N*-benzylidene-2-diazo-2-cyanoacethydrazide **3**. We found that this compound was unstable in organic solvents and underwent slow cyclisation to 1-benzylideneamino-5-hydroxy-1,2,3-triazole-4-carbonitrile **4**. The ^{13}C NMR spectrum correlates with the cyclic structure of **4**: it contains signals at 101.8 and 153.4 ppm, corresponding to the 4-C and 5-C atoms of 5-hydroxytriazoles.[4]

As in the case of diazomalonamides,[5] cyclisation of compound **3** is accelerated by the addition of bases, and the use of sodium ethylate leads to the formation of sodium 1-benzylideneamino-4-cyano-1,2,3-triazol-5-olate **5**. The interaction of **5** with hydrazine results in the removal of benzylidene protection and formation of sodium 1-amino-5-cyano-1,2,3-triazol-5-olate **6**. Upon addition of HCl (1 mol) to an aqueous solution of compound **6**, 2-cyano-2-diazoacethydrazide **8** is formed as a result of ring opening in a presumed intermediate, 1-amino-5-hydroxy-1,2,3-triazole-4-carbonitrile **7**. Thus, we have synthesised the first example of 2-diazomalonohydrazides.

To synthesise 2-ethoxycarbonyl and 2-methylcarbamoyl derivatives of 2-diazoacethydrazide, we studied the interaction of hydrazones of 2-ethoxycarbonyl- and 2-methylcarbamoyl-acethydrazides **9** and **10** with tosyl azide in the presence of sodium ethylate ('diazo group transfer' reaction).[6] This reaction was found to result in the formation of sodium salts of 5-hydroxytriazoles **11** and **12**, but not of the expected 2-diazomalonohydrazones.

It is noteworthy that one could expect formation of two isomeric triazoles **12** and **17** in the reaction of methylcarbamoyl derivatives **10** with TsN_3 *via* cyclisation of the intermediate diazo compounds at the amide or hydrazide groups. It was found that this reaction yields only isomers **12**; *i.e.*, only heterocyclisation with the participation of diazo and hydrazide fragments is realised. Treatment of 1-benzylideneamino-1,2,3-triazoles **11** and **12** with hydrazine leads to high yields of 1-amino-1,2,3-triazol-5-olates **13** and **14**.

As in the case of compound **6**, diazohydrazides **15** and **16**, which are chain isomers of 5-hydroxy-1,2,3-triazoles, are formed in the reaction of sodium salts **13** and **14** with hydrochloric acid.

Thus, we have synthesised the first examples of 2-diazoacethydrazides **8**, **15** and **16**, and the products of their cyclisation: derivatives of 1-amino-5-hydroxy-1,2,3-triazoles **4**–**6** and **11**–**14**.† All new compounds have satisfactory elemental analyses, IR and NMR spectroscopic data.

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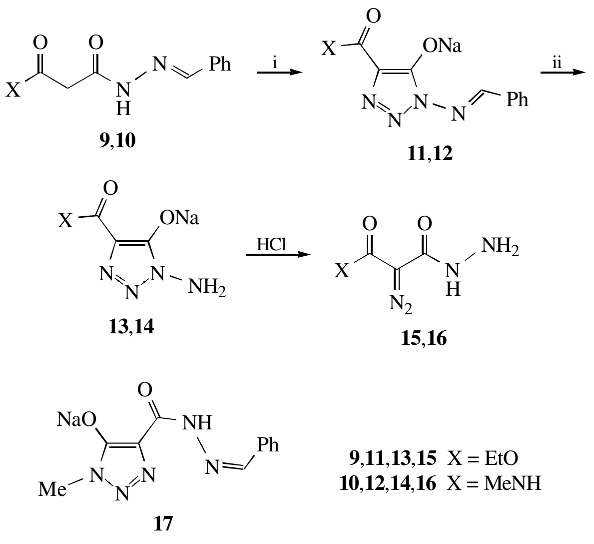

Scheme 2 *Reagents and conditions*: i, TsN_3, EtOH, EtONa; ii, EtOH, H_2NNH_2, 78 °C.

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† The ^{1}H and ^{13}C NMR spectra were recorded in [$^2H_6$]DMSO solution with a Bruker WH-250 spectrometer at 250 MHz, and the IR spectra were recorded in KBr using a UR-20 spectrometer.

Synthesis of **3** *and* **4**. A solution of amine **2** (4 g, 0.02 mol) in 12 ml of glacial acetic acid at 10–15 °C was treated with butyl nitrite (2.65 g, 0.025 mol). After stirring for 1 h, the precipitate **3** was filtered off. Recrystallisation of **3** from MeCN gives triazole **4**. Yield 2.22 g (52%), mp 162–164 °C (**CAUTION!** Explosive). ^{1}H NMR δ: 9.31 (s, 1H, N=CH), 12.31 (s, 1H, OH).

Synthesis of **5**. Compound **5** was obtained by treatment of **4** with an equimolar quantity of sodium ethylate in absolute ethanol with subsequent precipitation from diethyl ether. Yield 91%, mp 322–324 °C. ^{1}H NMR δ: 9.32 (s, 1H, N=CH).

Synthesis of **11** *and* **12** was performed by a 'diazo group transfer' method.[6]

For **11**: yield 72%, mp 225 °C (from EtOH, decomp.). ^{1}H NMR δ: 9.29 (s, 1H, N=CH), 4.15 (m, 2H, OCH_2, *J* 6.9 Hz), 1.25 (m, 3H, Me, *J* 6.9 Hz).

For **12**: yield 93.7%, mp 240–245 °C (decomp.). ^{1}H NMR δ: 9.33 (s, 1H, N=CH), 7.89 (m, 1H, NH, *J* 4.8 Hz), 2.75 (d, 3H, NMe, *J* 4.8 Hz).

General method for the preparation of **6**, **13** *and* **14**. Compounds **5**, **11** or **12**, respectively (2 mmol) were mixed with dry ethanol (8 ml) and hydrazine (100%, 2 mmol) and refluxed for 12 h. The product was filtered and washed with ethanol.

For **6**: yield 46%, mp 285 °C (decomp.).

For **13**: yield 65%, mp 170–20 0°C (decomp.). ^{1}H NMR δ: 5.25 (br. s, 2H, NH_2), 4.13 (q, 2H, CH_2, *J* 7.0 Hz), 1.23 (t, 3H, *J* 7.0 Hz).

For **14**: yield 90%, mp 300–305 °C. ^{1}H NMR δ: 7.86 (q, 1H, CONH, *J* 4.6 Hz), 5.30 (s, 2H, NH_2), 2.72 (d, 3H, Me, *J* 4.6 Hz).

General method for the preparation of **8**, **15** *and* **16**. An aqueous solution of **6**, **13** or **14** was mixed with 1 equiv. of HCl. After evaporation of **8** and **15** solutions *in vacuo* to dryness the residue was extracted with ethanol. The product **16** was separated by filtration.

For **8**: yield 50%, mp 140 °C (decomp.). IR (ν/cm^{-1}): 2150 (N_2), 2250 (CN).

For **15**: yield 55%, mp 157–160 °C. ^{1}H NMR δ: 9.94 (br. s, 1H, NH), 5.5–7.5 (br. s, 2H, NH_2) 4.28 and 4.23 (2q, 2H, CH_2, *J* 7.2 Hz), 1.27 (t, 3H, Me, *J* 7.2 Hz). IR (ν/cm^{-1}): 2145 (N_2).

For **16**: yield 47%, mp 200–203 °C (decomp.). ^{1}H NMR δ: 7.87 (br. s, 1H, NH), 4.25 (br. s, 2H, NH_2), 2.75 (d, 3H, Me, *J* 4.0 Hz). IR (ν/cm^{-1}): 2115 (N_2).

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