A facile synthesis of imidazolidine-2,4,5-trione

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When glycoluril was oxidised with potassium persulfate, the main product was imidazolidine-2,4,5-trione. The structure of product was confirmed by IR, ESI, ^{1}H NMR and X-ray crystal structure determination.

Keywords: glycoluril, oxidation, imidazolidine-2,4,5-trione, potassium persulfate

Imidazolidine-2,4,5-trione is a useful intermediate which can be used to synthesise imidazo[1,2-a]pyridines, -pyrazines, -pyrimidines, and some other nitrogen-bridgehead fused heterocycles.[1] This compound was first prepared by Heinrich and Ernst in 1913 by the condensation of urea and oxalyl dichloride.[2] Several methods[3–5] have been developed subsequently for the preparation of imidazolidine-2,4,5-trione, but many of these require a toxic solvent, an expensive catalyst or a long reaction time.

Glycoluril is a rigid bicyclic molecule which is used as a bleaching activator in industry,[6,7] structural units for cucurbituril[8,9] and as raw material for explosives.[10] Recently, many methods for the construction of glycoluril have been reported,[11–16] but its oxidation has never been described. When we studied the oxidation of glycoluril, imidazolidine-2,4,5-trione instead of the expected dihydroxy glycoluril was obtained. We now report these results.

Results and discussion

Potassium persulfate ($K_2S_2O_8$) is a mild oxidant that has been widely used in organic chemistry[17] because of its safety and high efficiency. Kim *et al.*[18] have accomplished that the direct perhydroxylation of cucurbituril (CB[n]) using $K_2S_2O_8$ as an oxidant to yield $(HO)_{2n}$CB[n]. Consequently, we thought that the glycoluril may be oxidised by this reagent (Scheme 1).

Glycoluril was obtained by the condensation of urea and glyoxal according to the literature method[19] A solution of glycoluril and $K_2S_2O_8$ in water was stirred for 2 hours at 75 °C. A white solid, which is soluble in water and ethyl acetate, was obtained. Based on the characterisation of ^{1}H NMR, IR, and MS spectroscopy, its structure was imidazolidine-2,4,5-trione and was confirmed by X-ray diffraction (Fig. 1).

The optimal reaction conditions were identified (Table 1). The results showed that the effect of reaction temperature was important, and 75 °C was the best choice. The reaction could not be completed at low temperatures, and the refluxing temperature did not enhance the yield of product because of the decomposition of the raw material. The amount of oxidant was optimal at 1 equiv. and the reaction time was optimal at 2 h longer times did not improve the yield.

As shown in Figs 1 and 2, the structure of imidazole skeleton in imidazolidine-2,4,5-trione is not an envelope structure, all the atoms are in one plane. In the molecule, all C and N atoms are of *sp*^{3} hybridisation, and the structure of molecule is not a standard pentagon. In the crystal lattice, every molecule is linked to other four molecules by four adjacent O•••H–N hydrogen bonds, named quadruple hydrogen bonding. There are two hydrogen bonding donors and two hydrogen bonding acceptor in one molecule, the generality of multimers is in the DAAD sequence.[20]

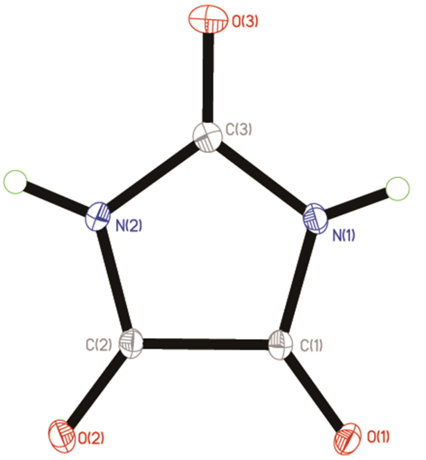
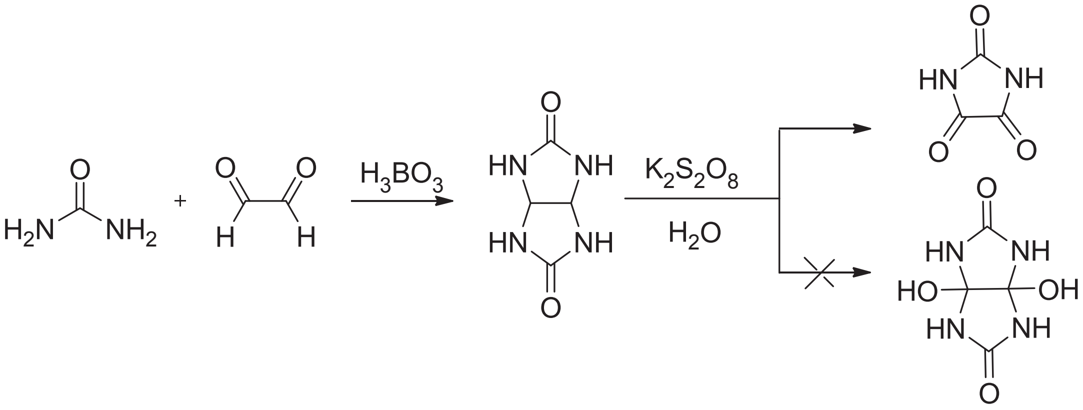


Fig. 1 Molecular structure of imidazolidine-2,4,5-trione at 30%probability thermal ellipsoids.



Scheme 1 Synthesis of imidazolidine-2,4,5-trione.

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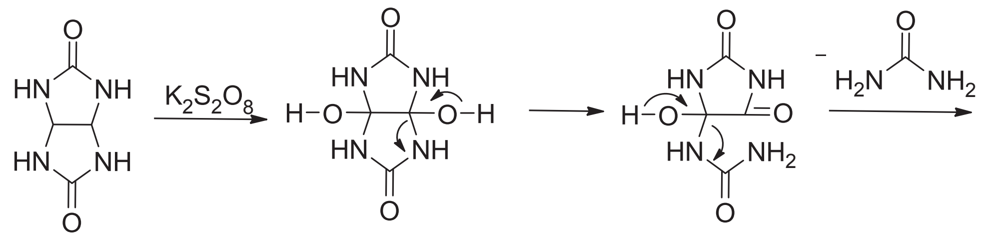

Scheme 2 Possible mechanism for the reaction.

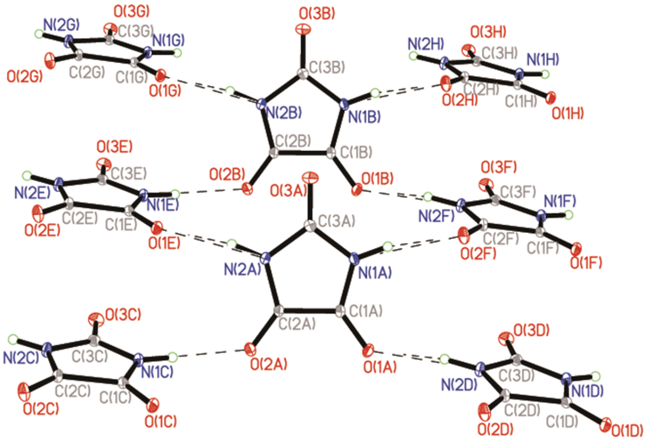

Fig. 2 The interactions between molecules.

The possible mechanism for the reaction is shown in Scheme 2. The protons of the glycoluril were firstly oxidised to hydroxy, then dihydroxy glycoluril was not stable and transformed to imidazolidine-2,4,5-trione.

In conclusion, this method is especially useful for the preparation of imidazolidine-2,4,5-trione from glycoluril under extremely mild conditions. The present methodology offers several advantages such as excellent yield, short reaction time, operational simplicity and mild conditions. The structure of the product was characterised by IR, ESI and ^{1}H NMR, and confirmed by X-ray crystal analysis.

Experimental

All commercial reagents and solvents were purchased and used in chemical grade without further purification. Melting point was determined using XT4A micro-scope melting point apparatus (uncorrected). IR spectra were recorded on a PerkinElmer FTIR spectrophotometer with KBr pellets. ^{1}H NMR spectra were recorded at a Varian mercury-plus 400 spectrometer with TMS as the internal standard. Mass spectra were recorded on a Varian 500-MS using ESI ionisation.

General procedure

Glycoluril (1 mmol) was added in 5 mL of distilled water. Then $K_2S_2O_8$ (1 mmol) was added to the solution and the system were stirred for 2 hours at 75 °C. The reaction mixture was extracted by ethyl acetate (5 mL × 3) and evaporated under reduced pressure. The product was recrystallised from petroleum/ethyl acetate to give a colourless single crystal which was suitable for X-ray diffraction analysis. The X-ray crystal structure was identical to that described previously.[21]

Imidazolidine-2,4,5-trione: White solid; yield 95%; m.p. 238–240 °C (1it.[22] 236–240 °C); IR (KBr, cm^{-1}): 3052, 2708, 2488, 1745, 1377, 1341, 1230, 993; ^{1}H NMR: (400 MHz, DMSO-d_6) δ_H 11.75 (2H, br); ESI *m/z* 114 (M$^+$, 100), 86(70), 43(39).

Table 1 Optimal conditions for the synthesis of imidazolidine-2,4,5-trione[a]

Entry	Temp/°C.	$K_2S_2O_8$/mmol	Time/h	Yield/%
1	RT	1	4	0
2	20	1	4	15
3	40	1	4	38
4	75	1	2	95
5	75	2	4	93
6	Reflux	2	2	80

[a]Conditions: Glycoluril (1 mmol, 1.42 g), distilled water (5 mL).

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