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Diaminomethyleneaminocarbonyldinitromethane, formed during the preparation of 2-amino-6-chloro-5-nitro-4(3*H*)-pyrimidinone by nitration of 2-amino-6-chloro-4(3*H*)-pyrimidinone

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Abstract—Difficulties in the nitration of 2-amino-6-chloro-4(3*H*)-pyrimidinone to give the widely used heterocyclic precursor 2-amino-6-chloro-5-nitro-4(3*H*)-pyrimidinone are shown to be due to formation of an unusual open-chain *gem*-dinitro compound, identified as diaminomethyleneaminocarbonyldinitromethane. The latter is also formed by the nitration of 2-amino-4,6(3*H*,5*H*)-pyrimidinedione. It decomposes with loss of carbon dioxide in dimethyl sulfoxide, or in aqueous potassium hydroxide, to give guanidine and dinitromethane.

2-Amino-6-chloro-5-nitro-4(3*H*)-pyrimidinone **2** is an important intermediate in heterocyclic synthesis and is the key starting material for the regiospecific Boon and Leigh synthesis of pteridines that has been used in the preparation of a wide variety of biologically important and drug related compounds.[1–3] It was first prepared by Davoll and Evans by the nitration of 2-amino-6-chloro-4(3*H*)-pyrimidinone **1** with concentrated nitric and sulfuric acids,[4] but the reaction is a difficult one, and several variations of the original experimental procedure have been published.[4,6–8] We wish to report that depending upon the reaction conditions used, the desired product **2** is frequently contaminated by substantial amounts of a second product, which we show to be the unusual *gem*-dinitro compound **3**. For example, when **1** is nitrated with fuming nitric acid in concentrated sulfuric acid at 0–10°C for 3 hours, the product obtained is **2** containing a small amount of **3**. On the other hand, if the same reaction mixture is left for 72 hours at 20°C, the only product obtained is the new compound. This new compound **3** is also formed by extended nitration of **2**, showing that under more vigorous nitrating conditions hydrolysis of the 6-chlorine atom occurs, together with cleavage of the pyrimidine ring and loss of carbon dioxide. Nitration of **1** with a 1 M ratio of KNO_3 in sulfuric acid at room temperature can also give 2-amino-6-chloro-5-nitro-4(3*H*)-pyrimidinone **2**. These conditions are milder and less hazardous than the usual concentrated/fuming nitric and sulfuric acid mixtures,[4–8] but here as well, the product obtained depends upon the exact reaction conditions. For example, after 3 hours, the major product is **2**, whereas after 72 hours all chlorine is lost from the molecule and the only product obtained is 2-amino-5-nitro-4,6(3*H*,5*H*)-pyrimidinedione **5**. Small amounts of this compound **5** have been reported previously as a by-product in the nitration of **1** with concentrated nitric/sulfuric acids.[5] Further nitration of it leads to the open chain *gem*-dinitro compound **3**, presumably via the dinitro intermediate **6**. None of the latter dinitro compound could be isolated, but small amounts of it were present in a sample of **3** prepared by nitration of the mononitro compound **5**, as shown by the negative ion electrospray mass spectrum, which contained a peak at m/z 216 ($M-H^+$). The easiest route to the new open-chain *gem*-dinitro product **3** is by the nitration of 2-amino-4,6(3*H*,5*H*)-pyrimidinedione **4** with excess KNO_3 in sulfuric acid. This reaction proceeds via the mono and dinitro pyrimidines **5** and **6**, since use of a 1 M ratio of KNO_3 allowed isolation of the mononitro intermediate **5**. Further details of the above reactions are summarised in Table 1. The new compound **3** is an insoluble bright yellow solid, and may easily pass undetected and cause trouble if **2** is being prepared for use as a reagent. It may be distinguished readily from **2**, however, by HPLC (cyano column, $MeOH/H_2O$), and by its high wavelength UV absorption band, $\lambda_{max.}$ 370 nm in 0.1 M NaOH; (ε 16,130).

Keywords: pyrimidines; nitration; *gem*-dinitro; dinitromethane; ring cleavage.

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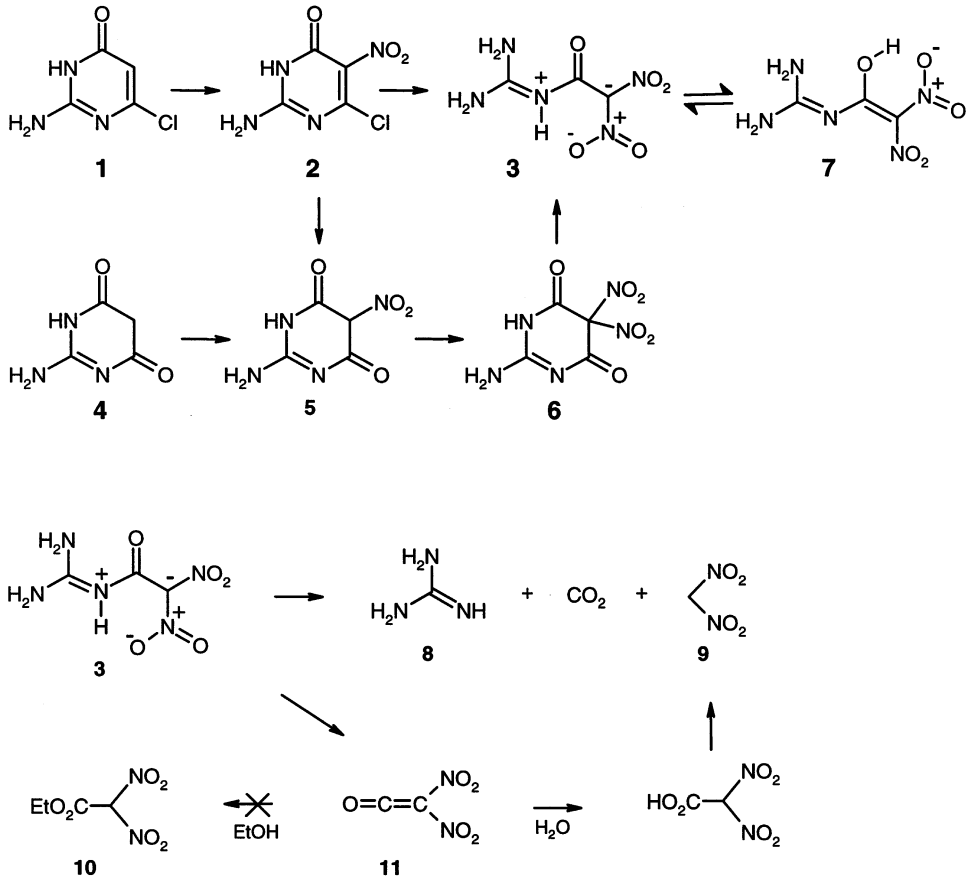

The structure of **3** is established by the following experimental data. Its ^{1}H NMR spectrum shows three signals, corresponding to five protons [δ_h 400 MHz, DMSO-d_6, 8.06 (s, 2H), 8.77 (s, 2H) and 11.41 (s, 1H)], while its ^{13}C NMR spectrum shows three signals, consistent with the presence of three carbon atoms (δ_c 100 MHz, DMSO-d_6, 134.54, 154.98 and 156.69). None of the carbon atoms in **3** carries any attached hydrogen atoms, as shown by the fully coupled spectrum. The carbon atom giving rise to the signal at δ 134.54 carries two nitro groups, since it appears as a triplet if **3** is prepared from **4** by nitration with labelled $K^{15}NO_3$ and as a doublet if prepared from unlabelled **5** with $K^{15}NO_3$. Presence of the extended chromophore in **3** is shown by its UV absorption maximum at 370 nm (0.1 M NaOH) and 320 nm (MeOH). An IR absorption band occurs at 1690 cm^{-1} (nujol). Finally, the high-resolution electrospray positive ion mass spectrum of **3** shows a main peak at m/z 192.0372 ($M+H^+$), (calcd. for $C_3H_6N_5O_5$ 192.0369). This molecular formula was confirmed by microanalysis (found: C, 18.91; H, 2.64; N, 35.99, calcd. for $C_3H_5N_5O_5$: C, 18.86; H, 2.64; N, 36.65). Negative ion electrospray mass spectrum shows a peak at m/z 190 ($M-H^+$). Of the various tautomeric forms possible for this compound, both the zwitterionic form **3** and the enolic form **7** fit the above data. Other tautomers are ruled out by the observation that none of the carbon atoms carries a hydrogen atom.

The new guanidinium *gem*-dinitro compound **3** is a stable solid at room temperature, and shows no sign of exploding in a mp tube at 360°C. On heating at 100°C for 1 hour in 1 M aqueous KOH it is hydrolysed with loss of carbon dioxide, and the potassium salt of dinitromethane **9** can be isolated from the reaction mixture (mp 215°C (explosive), lit.[9] 220°C (expl.), lit.[10] 208°C (expl.), δ_h 400 MHz, DMSO-d_6 8.16; δ_c 100 MHz, DMSO-d_6 122.02). Compound **3** decomposes within 3 days at room temperature in DMSO solution, and in 1 hour at 70°C in the same solvent. This decomposition in DMSO also involves loss of carbon dioxide, and may be followed by NMR, when the original three ^{1}H signals at δ 8.06, 8.77 and 11.41 become replaced by two signals at δ 8.17 and 6.93, and the original three ^{13}C signals at δ 134.54, 154.98 and 156.69 become replaced by two signals at δ 122.10 and 157.89. The signal at δ 157.89 is due to the guanidinium carbon atom. The signal at δ 122.10 is due to the anion of dinitromethane **9**, and appears as a doublet in a fully coupled spectrum, and as a triplet in a C–H decoupled spectrum if both nitro groups in the starting material **3** are ^{15}N labelled. Product **9** may be separated as a single peak on HPLC, and its high resolution electrospray negative ion mass spectrum, shows a peak at m/z 232.9774 ($2M-2H^++Na^+$), (calcd. for $C_2H_2N_4NaO_8$ 232.9770). A possible intermediate in the decomposition of **3** might be the ketene **11**, which on reaction with water would give dinitroacetic acid, which in turn would decarboxylate to give **9**. However, warming **3** in DMSO (dried over 4 Å molecular sieve) containing ethanol (dried over 3 Å molecular sieve) afforded no trace of the ethyl ester **10**, so that it is more likely that

Table 1. Nitration of pyrimidines with KNO_3 in sulfuric acid

Reaction	Starting pyrimidine mg (mmol)	H_2SO_4 (ml)	KNO_3 mg (mmol)	Time (h)	Product mg (mmol)	Yield (%)
(1)→(2)	291 (2.00)	2.0	202 (2.00)	1.5	275 (1.44)	72
(1)→(5)	291 (2.00)	2.0	202 (2.00)	72	266 (1.55)	77
(2)→(3)	40 (0.21)	0.5	65 (0.64)	10	35 (0.18)	87
(4)→(3)	254 (2.00)	4.0	607 (6.00)	2.5	325 (1.70)	85
(4)→(5)	510 (4.01)	20.0	405 (4.01)	2	554 (3.22)	80
(5)→(3)	90 (0.52)	2.0	210 (2.08)	8	80 (0.42)	81

The KNO_3 (anhydrous) was added in small portions to a stirred solution of the starting pyrimidine in concentrated sulfuric acid. The resulting solution was stirred at room temperature and then poured on to ice. The solid product was filtered off, washed with water, ethanol, diethyl ether, and dried in vacuo.

3 is hydrolysed by direct attack of nucleophile on the carbonyl carbon atom. These reactions are similar to those reported recently by Bergman, Latypov and co-workers in the nitration of barbituric acid,[11] although in this case it was possible to isolate 5,5-dinitrobarbituric acid as a stable solid.

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