On the Reaction of 3,4-Dihydropyrimidones with Nitric Acid. Preparation and X-Ray Structure Analysis of a Stable Nitrolic Acid [1]

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A series of substituted 3,4-dihydro-2-pyrimidones (DHPMs) was reacted with nitric acid under different reaction conditions. Treatment of DHPMs with 50-65% nitric acid at 0 °C led to the formation of the corresponding dehydrogenated 2-pyrimidones in moderate to good yields. In contrast, reaction of one representative DHPM with 60% nitric acid at 50 °C led to an unusually stable nitrolic acid, involving a formal nitration, nitrosation, and dehydrogenation step. The molecular structure of this product was determined by X-ray crystallographic analysis

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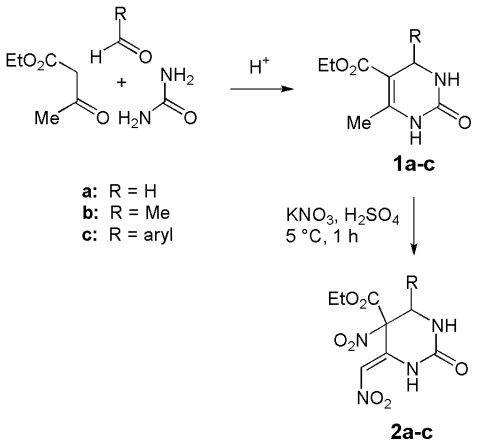
Introduction.

The search for new energetic compounds with combined high efficiency and low sensitivity is of considerable current interest [2]. In recent years attention focused particularly on pernitrated azaheterocycles [2-6] which in some cases can be directly obtained by exhaustive nitration of the corresponding heterocyclic scaffolds [7-10].

Some years ago we have reported on the nitration of dihydropyrimidones of the Biginelli-type (DHPMs), *i.e.* compounds **1** [11]. These heterocycles are readily available by acid-catalyzed three-component condensation of β-ketoesters, aldehydes, and ureas (Biginelli condensation, Scheme 1) [12,13]. Using potassium nitrate (2 equivalents) in concentrated sulfuric acid at 5 °C as nitration medium, the corresponding 5-nitro-4-(*Z*)-nitromethylidene pyrimidones **2a,b** were obtained from DHPMs **1a,b** (R = H, Me). In the case of the C4-phenyl substituted pyrimidone **1c** (R = phenyl), nitration of the aromatic ring also occurred under these conditions (using 3 equivalents KNO_3), providing mixtures of the *para*- and *meta*- substituted products **2c** (R = nitrophenyl). The structure and intramolecularly hydrogen-bonded (*Z*)-configurated geometry was established by an X-ray analysis of **2a** [11].

Scheme 1



In the present paper we discuss the reaction of DHPMs with nitric acid under different reaction conditions leading selectively either to dehydrogenated products or to the formation of nitrolic acids.

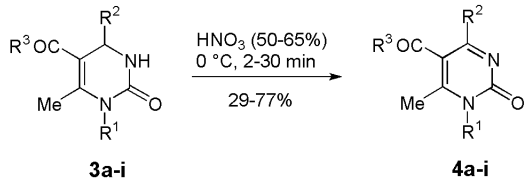
Results and Discussion.

Our initial investigations focused on the treatment of DHPMs **3a** with nitric acid of various concentration levels (50-65% HNO_3) and at different reaction temperatures. After some experimentation we discovered that a clean product can be obtained by simple addition of the solid DHPM **3a** to 60% HNO_3 at 0 °C. After basic work-up that removed small amounts of an acidic by-product (see structure **5** below) a colorless substance was obtained in 77% isolated yield after crystallization, that was readily identified on the basis of analytical data as the dehydrogenated pyrimidone **4a**. In the ^{1}H nmr spectrum, for example, the characteristic doublet of the C4 hydrogen at *ca*. 5.3 ppm in DHPM **3a** disappeared. In addition, the mass spectrum showed a peak for the molecular ion at *m/z* 259 (M+1), confirming the dehydrogenated structure **4a**. In the ^{13}C nmr broad signals were observed for some carbon atoms due to tautomerism (see structure **4A** in Scheme 5). The transformation **3** → **4** was initially surprising since we had previously experienced that dihydropyrimidones of the Biginelli-type are exceedingly difficult to oxidize (*i.e.* dehydrogenate) [14]. Such DHPMs have proven to be quite stable towards a variety of oxidizing agents such as sodium nitrite in acetic acid, pyridinium chlorochromate (PCC), cerium ammonium nitrate (CAN), manganese dioxide, potassium permanganate/clay, tetrachloro-1,4-benzoquinone (chloranil), and 2,6-dichloro-3,5-dicyanobenzoquinone (DDQ) [14]. So far no preparatively useful general procedure for the direct oxidation of Biginelli compounds has been reported [12]. In fact, only a single example in the patent literature refers to the use of nitric acid for this purpose [15].

We have therefore expanded the scope of this process and have tried these novel dehydrogenation conditions on a diverse set of functionalized DHPMs **3a-h**. As can be

seen from the data presented in Table 1, the method in general provides moderate to good yields (29-77%) of pyrimidones **4a-h**. However, a fine-tuning of the conditions with respect to the HNO_3 concentration and the reaction time was necessary in every case. As a general trend, dihydropyrimidones that bear an alkyl group at the C4 position (*i.e.* **3b**) are oxidized more rapidly than the C4-aryl substituted analogs, requiring only 50% HNO_3 and 5 minute reaction time. Other factors such as steric hindrance of the C4 position (as in **3e**) or solubility of the starting materials may also play a role.

Scheme 2



3a-i **4a-i**

Table 1

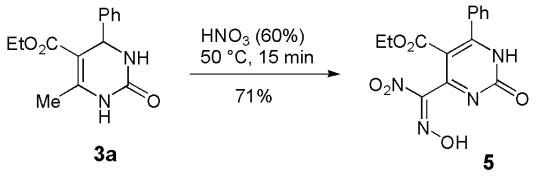
Isolated Yields and Reaction Conditions for the Oxidation of **3a-h** to **4a-h**

3,4	R^1	R^2	R^3	HNO_3 (%)	Time (min)	Yield (%)
a	H	C_6H_5	OEt	60	30	77
b	H	Me	OEt	50	5	54
c	H	4-NO_2-C_6H_4	OEt	65	10	59
d	H	3-Me-C_6H_4	OMe	60	15	76
e	H	2-CF_3-C_6H_4	OEt	65	30	29
f	Me	C_6H_5	OEt	60	10	65
g	Me	3-NO_2-C_6H_4	OCH_2Ph	50	30	76
h	H	C_6H_5	NEt_2	60	10	61

In order to promote conditions that would favor the formation of (per)nitrated products we have subsequently used higher reaction temperatures in these transformations involving nitric acid. Addition of solid DHPM **3a** to 60% nitric acid at 50 °C led after 15 minutes and subsequent aqueous work up to a nitrated product, as evidenced by elemental and ms analysis. Inspection of ^1H nmr and ^{13}C nmr data also indicated that a dehydrogenation process must have occurred. Final confirmation of the structure was obtained from an X-ray analysis, establishing the unusual nitrolic acid structure **5** (Figure 1). This compound, obtained in 71% isolated yield after crystallization, therefore is the result of a formal nitration, nitrosation, and dehydrogenation process (Scheme 3).

Nitrolic acids (α-nitro oximes) were first reported by Meyer in 1873 [16]. Since then, only scanty reports dealing with their synthesis, stability and use are found in the literature [17-26]. There have been some reports dealing with the rearrangement of nitrolic acids to *N*-nitroamides [18,19], and on their thermal fragmentation to nitrile

Scheme 3



3a **5**

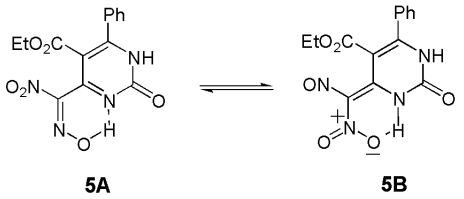
oxides at elevated temperatures [20,21]. All nitrolic acids and in particular the aromatic analogs appear to have low intrinsic stability and undergo a number of reactions, even when stored as solids at low temperatures [17-26]. In contrast, nitrolic acid **5** is a pale-yellow solid with an mp of 162-163 °C that can be recrystallized from boiling methanol/ethyl acetate. No decomposition was observed even upon prolonged storage as a solid at room temperature. Characteristically however, the mass spectrum of nitrolic acid **5** does not show the molecular ion peak (M+1) at 333, but only the mass of the corresponding nitril oxide (loss of "HNO_2") at 286 [20,21].

X-Ray Analysis of **5**.

The X-ray structure of **5** (Figure 1) unambiguously confirms the nitrolic acid structure and is only the second crystal structure determination of a nitrolic acid reported in the literature. Furthermore, beside the undissociated acetonitrolic acid [17] a zwitterionic dimethyl-ammonium nitrolate [45] and the salt furo[2,3-*c*]pyridinium 3-hydroxypyridine-4-nitrolate [46] are found in the Cambridge Structural Database [44]. In these structures, as well as in **5**, the nitrolic acid moiety adopts the characteristic *E* configuration which is likely to be a strong contributing factor towards the stability of this compound; *Z* configurated nitrolic acids are known to decompose much more rapidly [17]. Moreover, the hydroxyimino group and the nitro group are almost coplanar (*e.g.* 3.3° in **5**); solely in acetonitrolic acid the nitro group is markedly twisted (28.6°). By the planarity of the nitrolic acid group and the ethoxycarbonyl group at C5, the nitrolic acid moiety cannot be coplanar with the heterocyclic ring due to steric hindrance, but is twisted out of plane by 81.76(6)° (see Figure 1). Therefore an intramolecular hydrogen bond between H41 and N3 as indicated in structure **5A** is prevented. It should also be noted that the unambiguous location of the hydrogen atom on the oxime oxygen atom in the X-ray structure determination precludes the *gem*-nitrosonitromethylidene tautomer **5B** to be present in the solid state (Scheme 4) [27].

In the crystal the molecules of **5** form dimers *via* two hydrogen bonds lying around centers of symmetry between H1 and O2' of two pyrimidone rings (see Figure 1). These dimers are connected by hydrogen bonds between the H atoms of the nitrolic groups and N3" atoms forming a two-dimensional network of hydrogen bonded

Scheme 4



molecules. Folded sheets lying perpendicular to the crystallographic a-axis (see Figure 2) dominate the packing.

acid and dihydropyrimidone **3a** is somewhat unusual and deserves further comment, in particular due to the fact that under different reaction conditions (see Scheme 1) an entirely different product (involving nitration at C5) is obtained [11].

A mechanistic rationale for the formation of the various intermediates and products is presented in Scheme 5. The first step in the formation of the 5-nitro-4-(*Z*)-nitromethylidene pyrimidones **2** from DHPMs **1** and KNO_3/H_2SO_4 [11] is likely to be a nitration of the active methyl group at the C6 position of the pyrimidine ring by the nitronium cation

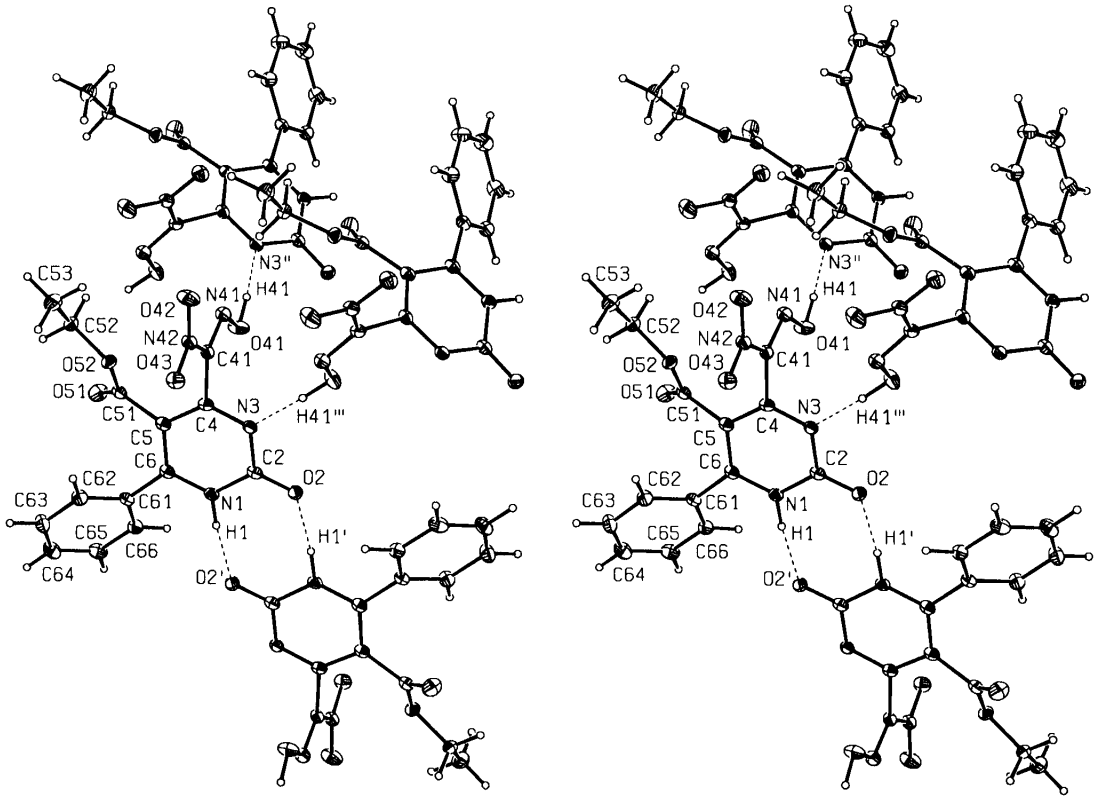


Figure 1. Stereoscopic ORTEP [43] plot of **5** showing the atomic numbering scheme and the hydrogen bonds to three other symmetry related molecules plotted with dashed lines. Symmetry codes: (') 2-x, 1-y, 2-z; (") x, 3/2-y, z-1/2; ("') x, 3/2-y, z+1/2. The probability ellipsoids are drawn at the 50% probability level.

Mechanistic Considerations.

Nitrolic acids (α-nitro oximes) can be synthesized by a number of methods [17-26]. In many cases the corresponding oximes are nitrated, or nitro derivatives nitrosated [17-26]. To our knowledge, the one-step formation of nitrolic acid derivatives by derivatization of a simple methyl group has been reported only in one case [28]. Here, 2-methyl-1,4-benzoxazin-2-one was treated with nitrous gases (prepared by reaction of nitric acid with sodium nitrite) in acetic acid at 35 °C to furnish the corresponding nitrolic acid in 38% yield [28]. Despite this literature precedent the high yielding direct formation of nitrolic acid **5** from nitric

formed under these nitration conditions (**1** → **A**). In general, this methyl group in Biginelli DHPMs is readily attacked by electrophiles [12]. With elemental bromine in chloroform, for example, selective mono- and dibromination of the methyl group in **1** can be achieved at 0 °C [29]. It is therefore reasonable to assume that under the reaction conditions used here, involving the electrophilic nitronium species, a similar pathway is followed. In a subsequent step, the nitronium ion then adds at C5 (*i.e.* at the electron-rich α position of the cyclic enamide moiety) to produce the dinitrated structure **2**. It is interesting to note that in contrast to *e.g.* the bromination reaction, here a different regioselectivity is

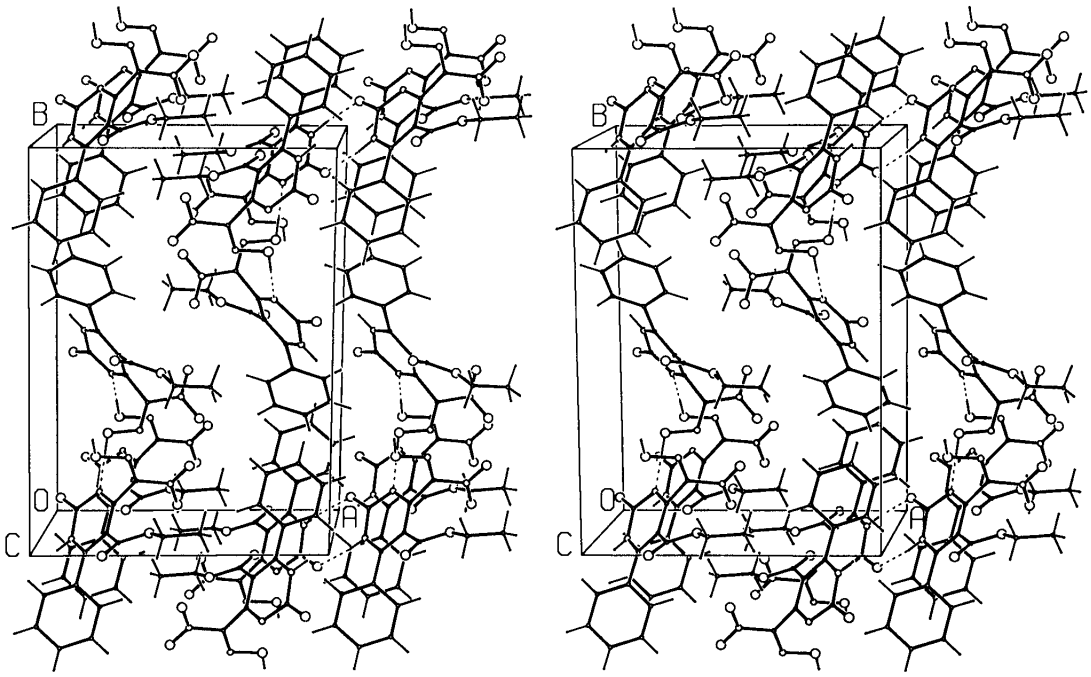


Figure 2. Stereoscopic ORTEP [43] plot of the packing of **5**. The atoms are drawn with arbitrary radii, the intermolecular hydrogen bonds are plotted with dashed lines.

Table 2

Selected Bond Lengths [Å] for **5**

N(1)-C(6)	1.348(2)
N(1)-C(2)	1.387(2)
C(2)-O(2)	1.221(2)
C(2)-N(3)	1.370(2)
N(3)-C(4)	1.317(2)
C(4)-C(5)	1.403(2)
C(4)-C(41)	1.495(2)
C(5)-C(6)	1.390(2)
C(5)-C(51)	1.493(2)
C(6)-C(61)	1.469(2)
C(41)-N(41)	1.266(2)
C(41)-N(42)	1.464(2)
N(41)-O(41)	1.3638(17)
N(42)-O(42)	1.2160(17)
N(42)-O(43)	1.2276(18)
C(51)-O(51)	1.196(2)
C(51)-O(52)	1.3396(19)
O(52)-C(52)	1.4599(19)
C(52)-C(53)	1.504(2)

Table 3

Selected Bond Angles [°] for **5**

C(6)-N(1)-C(2)	124.49(14)
O(2)-C(2)-N(3)	121.96(15)
O(2)-C(2)-N(1)	121.16(14)
N(3)-C(2)-N(1)	116.88(14)
C(4)-N(3)-C(2)	119.14(14)
N(3)-C(4)-C(5)	124.60(14)
N(3)-C(4)-C(41)	113.35(14)
C(5)-C(4)-C(41)	121.72(14)
C(6)-C(5)-C(4)	116.50(15)
C(6)-C(5)-C(51)	121.94(14)
C(4)-C(5)-C(51)	121.02(14)
N(1)-C(6)-C(5)	117.66(14)
N(1)-C(6)-C(61)	117.19(14)
C(5)-C(6)-C(61)	125.13(15)
N(41)-C(41)-N(42)	115.63(13)
N(41)-C(41)-C(4)	126.39(14)
N(42)-C(41)-C(4)	117.96(13)
C(41)-N(41)-O(41)	111.13(13)
N(41)-O(41)-H(41)	104.2(15)
O(42)-N(42)-O(43)	125.49(14)
O(42)-N(42)-C(41)	119.00(13)
O(43)-N(42)-C(41)	115.51(12)
O(51)-C(51)-O(52)	125.19(15)
O(51)-C(51)-C(5)	124.42(14)
O(52)-C(51)-C(5)	110.34(13)
C(51)-O(52)-C(52)	115.78(13)
O(52)-C(52)-C(53)	107.45(14)

Table 4

Selected Torsional Angles [°] for **5**

N(3)-C(4)-C(41)-N(41)	79.1(2)
C(5)-C(4)-C(41)-N(41)	-94.6(2)
N(3)-C(4)-C(41)-N(42)	-99.24(16)
C(5)-C(4)-C(41)-N(42)	87.06(19)
C(4)-C(41)-N(41)-O(41)	0.7(2)
N(41)-C(41)-N(42)-O(42)	3.8(2)
C(4)-C(41)-N(42)-O(43)	2.1(2)
C(6)-C(5)-C(51)-O(51)	-35.7(2)
C(6)-C(5)-C(51)-O(52)	146.60(14)
O(51)-C(51)-O(52)-C(52)	-5.9(2)
C(51)-O(52)-C(52)-C(53)	164.13(13)
C(5)-C(6)-C(61)-C(62)	-41.2(2)

Table 5

Hydrogen Bonding Geometries [Å, °] for **5**

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
N(1)-H(1)···O(2)'	0.93(2)	1.82(2)	2.7424(18)	173(2)
O(41)-H(41)···N(3)"	0.96(3)	1.67(3)	2.6322(18)	177(3)

Symmetry transformations used to generate equivalent atoms:
(') 2-x, 1-y, 2-z (") x, 3/2-y, z-1/2

observed, not yielding the expected *gem*-dinitro isomer **B**/**C**. For chlorinations of related DHPMs with $PCl_5/POCl_3$ however, the same regiochemistry (*i.e.* the formation of a 5-chloro-4-chloromethylidene derivative) has also been proposed [30]. In the case of dinitrated product **2** the protonating and highly acidic reaction conditions using concentrated sulfuric acid as solvent may also play an important role [11].

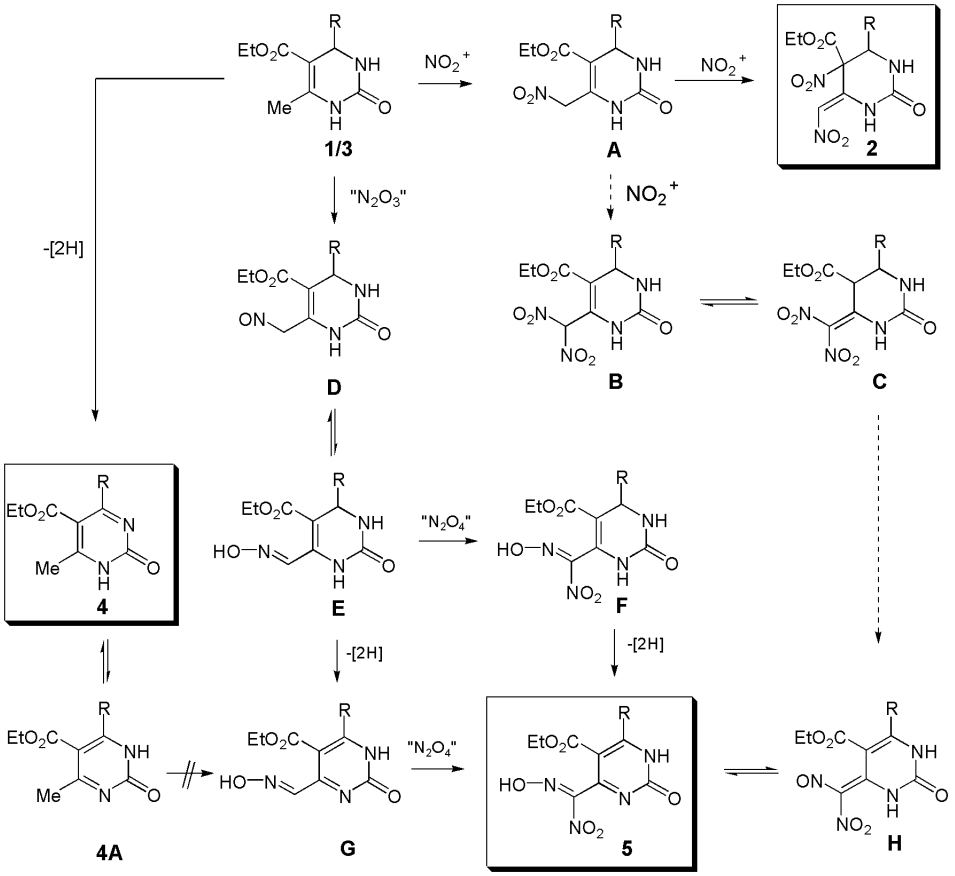
For the reaction of DHPM **3** involving concentrated nitric acid at 50 °C we suggest a different reaction pathway, not involving initial nitration of the C6 methyl group. In contrast, we propose that the first step here is a nitrosation of the active methyl group, in which the resulting nitroso compound **D** should rearrange to the oxime tautomer **E**. Such nitrosation reactions of activated methyl groups by either nitric acid or nitrous gases ("N_2O_3") have been reported in the literature [28,31]. The oxime **E** may subsequently be directly nitrated by the action of nitric acid ("N_2O_4", Ponzio reaction [17,24,28,32,33]) to furnish nitrolic acid **F**, from which the target compound **5** can be derived by dehydrogenation under the oxidative conditions present in the reaction medium. Alternatively, the oxime **E** may first be dehydrogenated and subsequently nitrated (**E** → **G** → **5**). The mechanism proposed here for the transformation of DHPM **3** to nitrolic acid **5** essentially follows the mechanism suggested by Biekert and Kössel for a related nitrolic acid formation [28]. In most cases described in the literature the obtained nitrolic acids are not stable and are readily transformed into furoxanes *via* nitrile oxide intermediates [17-28,31-33].

Finally, treatment of DHPMs **3** with 60% HNO_3 at 0 °C follows the standard radical oxidation (dehydrogenation) pathway, leading to pyrimidone **4** [34]. Importantly, this oxidized species is not an intermediate in the formation of nitrolic acid **5**, as confirmed by independent studies subjecting a sample of pyrimidone **4** to the HNO_3/50 °C reaction conditions. The oxidation must therefore occur *after* an initial nitration/nitrosation step.

An alternative mechanistic pathway to nitrolic acid **5** is also presented in Scheme 5. If one would assume that dinitration of DHPM **1** at 50 °C (60% HNO_3) leads to *gem*-dinitro pyrimidone **B**/**C**, an internal redox process would readily furnish nitrolic acid **5**. Although there is literature precedent for the *gem*-dinitration of active methylene and methyl groups [8,35-37], we are not aware of any precedent for a (non-photochemical [38-41]) redox process such as the hypothetical **C** → **H** transformation.

In conclusion, we have demonstrated that depending on the reaction conditions nitric acid can either dehydrate DHPMs to the corresponding 2-pyrimidones (**3** → **4**), or convert the C6-methyl group into an unusually stable nitrolic acid function (**3** → **5**). The further pernitration of these and the related nitromethylidene systems **2** is currently under investigation.

Scheme 5



EXPERIMENTAL

Melting points were obtained on a Gallenkamp melting point apparatus, Model MFB-595 in open capillary tubes. The ^{1}H and ^{13}C nmr spectra were obtained on a Bruker AM360 instrument at 360 and 90 MHz, respectively. Chemical shifts in ^{1}H nmr spectra are reported in ppm from internal tetramethylsilane and are given in δ units. The solvent for ^{1}H nmr was hexadeuteriodimethylsulfoxide unless otherwise stated. Microanalyses were performed on a Carlo Erba 1106 elemental analyzer. Infrared spectra were taken on a Perkin-Elmer 298 spectrophotometer in potassium bromide pellets. Mass spectra were acquired on a Hewlett-Packard LC/MSD 1100 series instrument in the atmospheric pressure ionization (API) mode. Nitric acids of various concentrations were prepared by dilution of concentrated (65%) nitric acid. DHPMs **3a-h** were prepared according to literature procedures [12].

General Procedure for the Dehydrogenation of DHPMs **3a-h** with Nitric Acid.

To a stirred and cooled (0 °C) quantity of nitric acid (6.5 mL, for concentration see Table 1) the appropriate DHPMs **3a-h** (4 mmoles) were added portionwise within 5 minutes as solids. After being stirred for an additional 2 minutes under cooling, the mixture was allowed to gradually warm to room temperature within 2-30 minutes (for individual reaction times see Table 1) the mixture was poured onto crushed ice (*ca*. 10 g), and then treated with solid potassium carbonate until a pH of 8 was reached. The resulting aqueous solution was subsequently extracted with chloroform (3 x 30 mL), the organic layer dried over sodium sulfate, and evaporated to dryness. The residual crude product was purified by recrystallization from the appropriate solvent (see below) to give the corresponding pure pyrimidones **4a-h**.

Ethyl 6-Methyl-2-oxo-4-phenyl-1,2-dihydropyrimidine-5-carboxylate (**4a**).

This compound was obtained as colorless solid (ethanol), mp 191-192 °C; ir: 3150-2600 (NH), 1730 (C=O), 1650 (C=O), 1600 cm^{-1}; ^{1}H nmr: δ 0.82 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.38 (s, 3 H, CH_3), 3.95 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.48 ppm (m, 5 H, Ph); ^{13}C nmr: δ 13.3, 18.4, 61.3, 128.3, 129.1, 131.0, 137.0, 156.41, 166.9 ppm; ms: *m/z* 259 (M+1), 231, 213.

Anal. Calcd for $C_{14}H_{14}N_2O_3$ (258.27): C, 65.11; H, 5.49; N, 10.90. Found: C, 64.98; H, 5.49; N, 10.90.

Ethyl 4,6-Dimethyl-2-oxo-1,2-dihydropyrimidine-5-carboxylate (**4b**).

This compound was obtained as colorless solid (ethanol), mp 155-157 °C; ir: 3150-2600 (NH), 1720 (C=O), 1665 (C=O), 1610 cm^{-1}; ^{1}H nmr: δ 1.26 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.31 (s, 6 H, 2 CH_3), 4.09 ppm (q, J = 7.5 Hz, 2 H, CH_2CH_3); ^{13}C nmr: δ 13.4, 21.0, 60.8, 108.8, 154.7, 164.9 ppm; ms: *m/z* 197 (M+1).

Anal. Calcd for $C_9H_{12}N_2O_3$ (196.21): C, 55.10; H 6.16; N, 14.28. Found: C, 54.97; H, 6.02; N, 14.20.

Ethyl 6-Methyl-4-(4-nitrophenyl)-2-oxo-1,2-dihydropyrimidine-5-carboxylate (**4c**).

This compound was obtained as pale yellow solid (ethanol), mp 217-218 °C; ir: 3150-2600 (NH), 1710 (C=O), 1645 (CO), 1590 cm^{-1}; ^{1}H nmr: δ 0.81 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.44 (s, 3 H, CH_3), 3.94 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.66 (d, J = 8.0 Hz, 2 H, ArH), 8.30 ppm (d, J = 8.0 Hz, 2 H, ArH).

Anal. Calcd for $C_{14}H_{13}N_3O_5$ (303.27): C, 55.44; H, 4.32; N, 13.86. Found: C, 55.15; H, 3.98; N, 13.61.

Methyl 6-Methyl-3-(3-methylphenyl)-2-oxo-1,2-dihydropyrimidine-5-carboxylate (**4d**).

This compound was obtained as colorless solid (ethanol), mp 175-177 °C; ir: 3150-2600 (NH), 1730 (C=O), 1645 (CO), 1600 cm^{-1}; ^{1}H nmr: δ 2.33 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 3.48 (s, 3 H, OMe), 7.22 ppm (m, 4 H, ArH).

Anal. Calcd for $C_{14}H_{14}N_2O_3$ (258.27): C, 65.11; H, 5.49; N, 10.90. Found: C, 64.82; H, 5.46; N, 10.78.

Ethyl 6-Methyl-2-oxo-4-(2-trifluoromethylphenyl)-1,2-dihydropyrimidine-5-carboxylate (**4e**).

This compound was obtained as colorless solid (ethanol), mp 193-195 °C; ir: 3150-2600 (NH), 1720 (C=O), 1660 (CO), 1590 cm^{-1}; ^{1}H nmr: δ 0.78 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.45 (s, 3 H, CH_3), 3.76 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.26-7.76 ppm (m, 4 H, ArH).

Anal. Calcd for $C_{15}H_{13}F_3N_2O_3$ (326.28): C, 55.22; H, 4.01; N, 8.58. Found: C, 55.15; H, 3.63; N, 8.70.

Ethyl 1,6-Dimethyl-2-oxo-4-phenyl-1,2-dihydropyrimidine-5-carboxylate (**4f**).

This compound was obtained as colorless solid (ethanol), mp 219-221 °C; ir: 1720, 1690, 1665 (C=O), 1600 cm^{-1}; ^{1}H nmr: δ 0.84 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.50 (s, 3 H, CH_3), 3.52 (s, 3 H, NCH_3), 3.97 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.48 ppm (m, 5 H, ArH); ^{13}C nmr: δ 13.3, 18.1, 32.9, 61.4, 119.6, 127.4, 128.5, 130.4, 138.4, 155,1, 160.6, 166.6, 169.5 ppm.

Anal. Calcd for $C_{15}H_{16}N_2O_3$ (271.31): C, 66.16; H, 5.92; N, 10.29. Found: C, 66.00; H, 6.02; N, 10.29.

Benzyl 1,6-Dimethyl-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyrimidine-5-carboxylate (**4g**).

This compound was obtained as pale yellow solid (ethanol), mp 162-165 °C; ir: 1710 (C=O), 1670 (C=O), 1590 cm^{-1}; ^{1}H nmr: δ 2.54 (s, 3 H, CH_3), 3.58 (s, 3 H, NCH_3), 5.01 (m, 2 H, OCH_2), 7.03-8.12 ppm (m, 9 H, ArH).

Anal. Calcd for $C_{20}H_{17}N_3O_5$ (379.37): C, 63.36; H, 4.52; N, 11.07. Found: C, 63.32; H, 4.55; N, 11.32.

N,N-Diethyl 6-Methyl-2-oxo-4-phenyl-1,2-dihydropyrimidine-5-carboxylic Acid Amide (**4h**).

This compound was obtained as colorless solid (ethanol), mp 149-152 °C; ir: 1660 (C=O), 1610 (C=O), 1580 cm^{-1}; ^{1}H nmr: δ 0.66 and 0.81 (2 t, J = 7.5 Hz, 6 H, CH_2CH_3), 2.24 (s, 3 H, CH_3), 2.76, 2.91, 3.17, 3.38 (4 m, 4 H, NCH_2CH_3), 7.52 ppm ppm (m, 5 H, ArH).

Anal. Calcd for $C_{16}H_{19}N_3O_2$ (285.35): C, 67.35; H, 6.71; N, 14.73. Found: C, 66.86; H, 6.66; N, 14.67.

Ethyl 4-(Hydroxyimino-nitro-methyl)-2-oxo-6-phenyl-1,2-dihydropyrimidine-5-carboxylate (**5**).

To a stirred quantity of 60% nitric acid (8.0 mL) solid DHPM **3a** (1.51 g, 5.80 mmoles) was added at 50 °C. After being stirred at 50 °C for 15 minutes the mixture was poured onto crushed ice (20 g). The solid precipitate was filtered, washed successively with water and ether, and dried. Recrystallization from methanol:ethyl acetate (1:2, v/v) produced 1.36 g (71 %) nitrolic

acid **5** as a pale yellow solid, mp 162-163 °C; ir: 3100-2200 (OH, NH), 1740 (C=O), 1685 (C=O), 1590, 1550 cm^{-1}; ^1H nmr (methanol-d_4): δ 0.88 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 3.95 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.54 ppm (m, 5 H, ArH); ^1H nmr (DMSO-d_6): δ 0.76 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 3.91 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 7.54 ppm (m, 5 H, ArH); ^{13}C nmr (DMSO-d_6): 17.3, 54.4, 102.1, 127.2, 128.3, 129.3, 144.3, 145.3, 167.9, 175.5; ms: *m/z* 286 (M+1, -HNO_2), 270, 258, 242, 104.

Anal. Calcd for $C_{14}H_{12}N_4O_6$ (332.27): C, 50.61; H, 3.64; N, 16.86. Found: C, 50.49; H, 3.55; N, 16.81.

X-Ray Structure Analysis of Nitrolic Acid **5**.

All the measurements were performed using graphite-monochromatized Mo K_α radiation at 90(2)K: molecular formula $C_{14}H_{12}N_4O_6$, M_r = 332.28, monoclinic, space group P $2_1/c$, a = 12.439(4)Å, b = 17.198(4)Å, c = 7.145(2)Å, β = 99.11(2)°, V = 1509.2(7)$Å^3$, Z = 4, d_{calc} = 1.462g cm^{-3}, μ = 0.117mm^{-1}. A total of 3941 reflections were collected (Θ_{max} = 26°), from which 2969 were unique (R_{int} = 0.0364), with 2498 having I > 2σ(I). The structure was solved by direct methods (SHELXS-97 [41]) and refined by full-matrix least-squares techniques against F^2 (SHELXL-97 [42]). The non-hydrogen atoms were refined with anisotropic displacement parameters. The H-atoms attached to the N or O atoms were refined without any positional constraints with isotropic displacement parameters. The other H-atoms were refined with common isotropic displacement parameters for the H-atoms attached to the same C atom or to the same phenyl ring, respectively, and with idealized geometries. For 228 parameters final *R* indices of R = 0.0398 and wR^2 = 0.1013 (GOF = 1.053) were obtained. The largest peak and hole in a difference Fourier map were 0.283 and -0.222e$Å^{-3}$, respectively.

Selected bond lengths and angles are listed in Tables 2-5. The atomic coordinates, displacement parameters, and further details of the crystal structure investigations are available on requests from the director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB2 1EZ (e-mail: deposit@ccdc.cam.ac.uk), on quoting the depository number CCSD-162255, the names of the authors, and the journal citation.

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