Synthesis and Crystal Structure of Triethylammonium 5-[(2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)(methylthio)methyl]-1,3-dimethylpyrimidine-2,4,6-trionate

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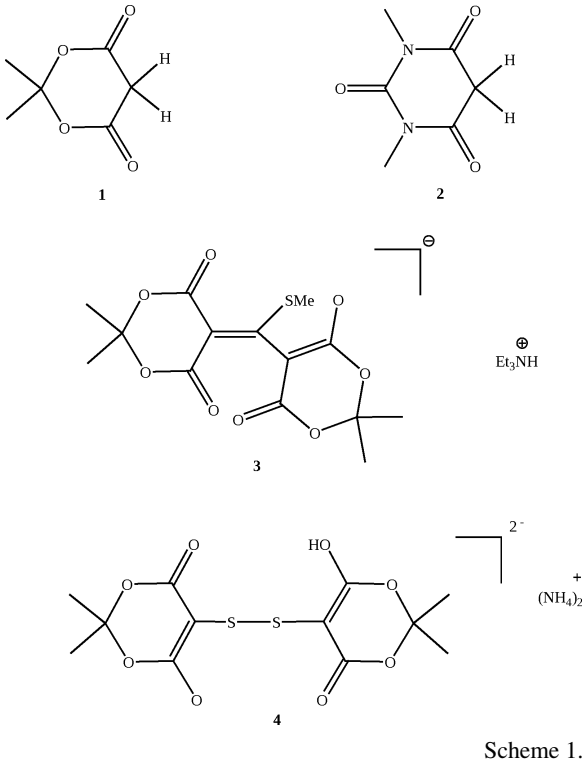
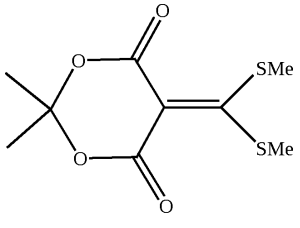
Triethylammonium 5-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)(methylthio)methyl]-1,3-dimethylpyrimidine-2,4,6-trionate (**6**) is obtained as red-orange stable crystals by reaction of 5-[bis(methylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**5**) with 1,3-dimethylbarbituric acid (**2**) in the presence of triethylamine in excellent yield. The crystal structure of **6** confirms the negative charge to be localized at the barbituric-acid ring in its enolate form.

Key words: Meldrum's Acid, 1,3-Dimethylbarbituric Acid, Heterocycles, Crystal Structure



Scheme 1.



Scheme 2.

Introduction

Meldrum's acid (**1**) and 1,3-dimethylbarbituric acid (**2**) are considered to be reactive organic compounds due to their high chemical affinity towards carbonyl compounds. Barbiturates are most widely used for sedative-hypnotic drugs [1]. Barbituric acid salts, in particularly sodium salts, are widely applicable as pharmaceuticals because they are soluble in water and can be used as intravenous injections [2].

In the course of our investigation on new organic derivatives of Meldrum's acid and 1,3-dimethylbarbituric acid, we isolated and characterized several examples of salts containing the Meldrum's acid fragment as in compounds **3** and **4**, or the 1,3-dimethylbarbituric acid fragment, exclusively [3 – 5] (Scheme 1).

Results and Discussion

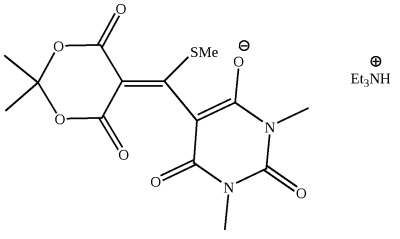
Synthesis and crystal structure of the salt ***6***

One of the most important derivatives of Meldrum's acid is the methylene compound **5** first prepared by Huang and Chen [6]. Its crystal structure has been determined by our group only recently [7] (Scheme 2).

Many studies [8 – 10] showed that one or two thiomethyl groups of compound **5** could be exchanged by

Table 1. Crystal data and structure refinement for $C_{20}H_{31}N_3O_7S$ (**6**).

Empirical formula	$C_{20}H_{31}N_3O_7S$
Formula weight, g mol^{-1}	457.54
Temperature, K	173(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a, Å	7.660(2)
b, Å	17.317(3)
c, Å	17.697(3)
V, Å^3	2347.3
Z	4
Radiation; λ, Å	MoK_α; 0.71073
Density, g cm^{-3}	1.295
μ(MoK_α),	0.182
F(000), e	976
Theta range for data collection	3.13 to 26.37°
hkl ranges	±9, ±21, ±22
Reflections collected	33054
Independent reflections	4799 (R_{int} = 0.104)
Reflexions with $I \geq 2\sigma(I)$	4526
Refinement method	Full-matrix least-squares on F^2
x(Flack)	0.00(6)
$R1$	0.034
$wR2$ (all data)	0.081
$\Delta\rho$ (max/min), e Å^3	+0.22/−0.16



6

Scheme 3.

nucleophilic organic groups. Reaction of **5** with 1,3-dimethylbarbituric acid (**2**) in the presence of triethylamine gives **6** as red-orange stable crystals in excellent yield (Scheme 3).

We have determined the crystal structure of **6** to get more insight into the bonding of the anion (Tables 1 and 2, Fig. 1). The crystal structure reveals the negative charge to be localized at the barbituric-acid ring in its enolate form [C(6)–C(7) 1.402(2), C(6)–C(8) 1.418(2), C(7)–O(7) 1.253(2), C(8)–O(8) 1.236(2) Å]. As a consequence, the barbituric-acid ring is linked to the central carbon atom C(5) by a single bond [C(5)–C(6) 1.467(2) Å]. In contrast, the Meldrum's acid ring is connected to C(5) by a double bond [C(3)–C(5) 1.375(2) Å], and its structure exhibits less extensive π-electron delocalization [C(2)–C(3) 1.465(2), C(3)–C(4) 1.480(3), C(2)–O(2) 1.206(2), C(4)–O(4) 1.198(2) Å]. This fact may be explained by the more efficient π-electron distribution in the barbituric-acid

Table 2. Selected bond lengths (Å) and angles (deg) for $C_{20}H_{31}N_3O_7S$ (**6**).

S(1)–C(5)	1.739(2)	N(2)–C(8)	1.414(2)
O(2)–C(2)	1.206(2)	C(3)–C(2)	1.465(2)
O(4)–C(4)	1.198(2)	C(3)–C(4)	1.480(3)
O(7)–C(7)	1.253(2)	C(5)–C(3)	1.375(2)
O(8)–C(8)	1.236(2)	C(5)–C(6)	1.467(2)
O(9)–C(9)	1.221(2)	C(6)–C(7)	1.402(2)
N(1)–C(7)	1.400(2)	C(6)–C(8)	1.418(2)
O(8)–C(8)–C(6)	125.69(16)	C(7)–C(6)–C(8)	121.87(16)
C(5)–C(3)–C(4)	120.82(16)	C(7)–C(6)–C(5)	119.67(16)
C(5)–C(3)–C(2)	122.00(16)	C(2)–C(3)–C(4)	117.07(16)
C(8)–C(6)–C(5)	117.90(15)	O(2)–C(2)–O(12)	118.15(16)
C(3)–C(5)–C(6)	121.07(15)	O(2)–C(2)–C(3)	124.52(17)
C(3)–C(5)–S(1)	119.99(13)	O(7)–C(7)–N(1)	117.60(17)
C(6)–C(5)–S(1)	118.85(13)	O(7)–C(7)–C(6)	125.45(17)
O(4)–C(4)–O(14)	117.53(17)	N(1)–C(7)–C(6)	116.95(16)
O(8)–C(8)–N(2)	118.71(16)	O(12)–C(2)–C(3)	117.31(16)
N(2)–C(8)–C(6)	115.57(15)	O(14)–C(4)–C(3)	115.49(15)
C(5)–S(1)–C(100)	104.35(9)	O(4)–C(4)–C(3)	126.77(18)

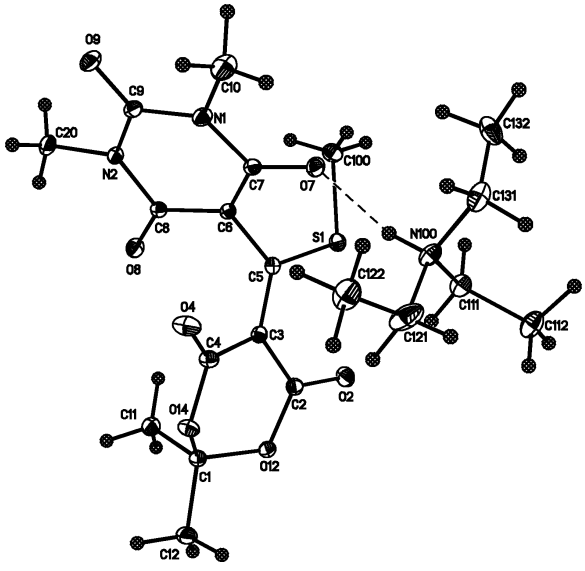
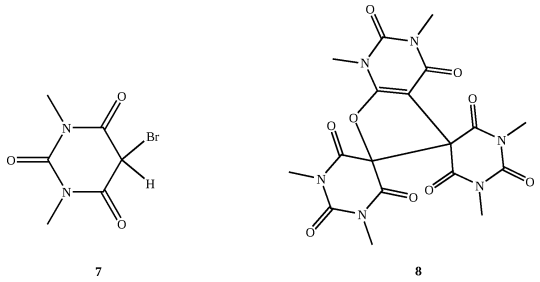


Fig. 1. View of the ion pair of $C_{20}H_{31}N_3O_7S$ (**6**) in the crystal.

fragment which approaches heteroaromaticity, though there are only minor differences in the pK_a values of both organic acids (4.83 and 4.76 for **1** and **2**, respectively).

Additional information about the charge comes from the structure of the ion pairs in the crystal. The cation is linked to one oxygen atom of the barbituric-acid fragment by a weak N–H$\cdots$O bond [N(100)–H(10g) 0.89(1), O(7)$\cdots$H(10g) 1.83(1) Å, N(100)–H(10g)$\cdots$O(7) 161(1)°], which may also cause the small difference in the C–O bonds of the barbituric-acid ring mentioned above.



Scheme 4.

*Reaction of **6** with 5-bromo-1,3-dimethylbarbituric acid (**7**)*

The trinuclear barbituric acid derivative **8** was obtained by reacting **6** with 5-bromo-1,3-dimethylbarbituric acid **7** in CH_3NO_2 as a solvent. Formation of a trimeric form of 1,3-dimethylbarbitric acid may be explained by *in situ* generation of a barbituric acid carbene intermediate, which can not be isolated (Scheme 4).

M. Poling and D. Helm reported on the X-ray crystal structure of **8** without any further analytical data or detailed information on the synthesis of this compound [11]. The Experimental Part (below) includes a convenient method to prepare **8** from **6** and the barbituric acid derivative **7**, and its characterization by MAS NMR spectroscopy.

Experimental Section

All starting materials were purchased from commercial sources and used without further purification. Experiments were performed in purified solvents under argon. Crystals of $C_{20}H_{31}N_3O_7S$ (**6**) were obtained by slow evaporation of a CH_2Cl_2 solution of **6**.

CCDC 671172 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk/data_request/cif.

*$C_{20}H_{31}N_3O_7S$ (**6**)*

To a solution of **5** (2.48 g, 10 mmol) and **2** (1.56 g, 10 mmol) in THF (30 mL) triethylamine (1.4 mL, 10 mmol) was added. The mixture was stirred at r. t. for 2 h, then THF was removed *in vacuo*. The resulting precipitate was stirred at r. t. in diethylether (30 mL) for another 3 h and the resulting precipitate was filtered to give 3 g (64 %) of **6** as stable red-orange crystals.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, 9 H, CH_2CH_3, ^3J = 7.0 Hz), 1.79 (s, 6 H, 2-Me_M), 2.25 (s, 3 H, SMe), 2.99 (q, 6 H, CH_2CH_3), 3.23 (s, 6 H, NMe_B), 10.60 (s, 1 H, NH). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 8.5 (CH_2CH_3), 16.8 (SMe), 26.7 (CMe_2), 27.89 NMe_B), 45.8 (CH_2CH_3), 88.3 (CMe_2), 104.6 ($C5_B$), 108.1 $C5_M$), 152.7 (CSMe), 160.8 ($C2_B$), 162.5 ($C4,6_M$), 179.6 ($C4,6_B$). – Elemental analysis for $C_{20}H_{31}N_3O_7S$ (457.54): calcd. C 52.50, H 6.83, N 9.18, S 7.01; found C 52.1, H 7.12, N 9.25, S 6.67.

*$C_{18}H_{18}N_6O_9$ (**8**)*

To a solution of **6** (2.33 g, 5 mmol) in CH_3NO_2 (10 mL) compound **7** was added (1.18 g, 5 mmol). The mixture was then stirred at r. t. for 3 h. The resulting precipitate was filtered to give 0.47 g (60 %) of **8** as stable crystals.

^{13}C NMR (400 MHz, MAS): δ = 26.37, 30.72 (NMe), 68.28, 84.67, 90.30, 149.71, 151.41, 158.51, 161.98, 163.90, 166.39 (CO, C=*C*(NMe)-O). – MS (EI, 70 eV): *m/z* (%) = 462 (5) $[M]^+$, 320 (100) $[M–C_5H_6N_2O_3]^+$, and further fragments. – Elemental analysis for $C_{18}H_{18}N_6O_9$ (462.38): calcd. C 46.76, H 3.92, N 18.18; found C 46.91, H 3.60, N 18.52.

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