

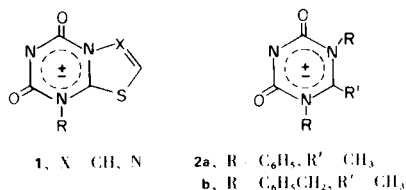
Mesoionic 1,3-Disubstituted *s*-Triazine-4,6-diones and Their Thione Derivatives (1a)

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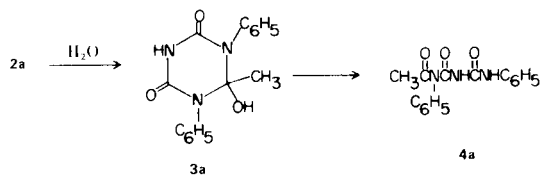
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We have previously described the syntheses of a number of mesoionic purinone analogs (2,3) including mesoionic xanthine analogs of type 1 (4). Compounds 1 may be regarded as ring-fused derivatives of the unknown mesoionic 1,3-disubstituted *s*-triazine-4,6-dione 2. We wish to report the synthesis of 2 and its thione derivatives.



Compounds 2a,b were synthesized by the reaction of *N,N'*-disubstituted acetamidines with phenoxy carbonyl isocyanate (5) in refluxing anhydrous toluene. Structure assignments are based upon elemental analyses and spectral evidence including: substantial downfield shift of methylene (or phenyl) proton signals of nitrogen substituents as a result of *N*-acylation, pseudocarbonyl group absorption at 1730 and 1689 cm⁻¹ comparable to that reported for examples of 1 (4), and the observation of parent molecular ions in the mass spectra. Several other derivatives of 2 were prepared in this manner (2c R = C₆H₅, R' = H, m.p. 236-237°; 2d R = R' = C₆H₅, m.p. 263-264°; 2e R = *p*-MeOC₆H₄, R' = CH₃, m.p. 249-250°), however, these proved to be too unstable to obtain in a state of analytical purity.

Although mesoionic *s*-triazinediones 2 are thermally stable, exposure to moisture leads to the formation of ring-opened products 4, presumably arising from a covalent hydrate intermediate 3. Thus, addition of a drop of water to a deuteriochloroform solution (0.5 ml.) of 2a resulted



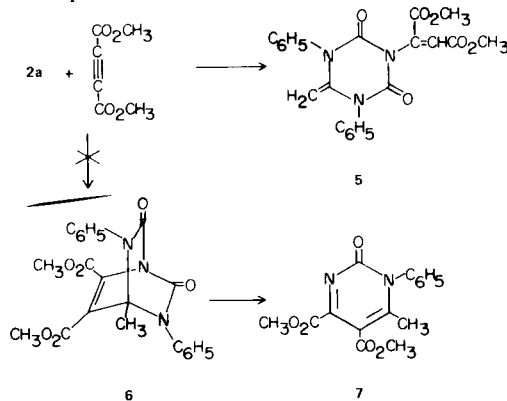
in the disappearance of the singlet at δ 3.18 assigned to the methyl group protons and the appearance of a new singlet

at δ 2.0 assigned to the methyl group protons of 4a. Attempts to isolate 3a by crystallization or chromatography were unsuccessful. Samples of 2a exposed to atmospheric moisture or solvents not rigorously dried became quickly contaminated with 4a. In general, samples of 2 first isolated from the reaction mixtures were of greater purity (as judged by melting points, absence of extraneous signals in the nmr spectra, and elemental analyses) than those obtained upon attempted recrystallization.

The mode of reaction of 2 with nucleophiles is consistent with the reported chemical properties of 5-azauracil derivatives (6-8). The susceptibility to nucleophilic attack at the 2-position is apparently enhanced in comparison to either 1 or 5-azauracil. In this regard, compounds 2 also appear to be somewhat less stable than their 5-deaza analog, mesoionic 1,3-disubstituted pyrimidine-4,6-diones (9).

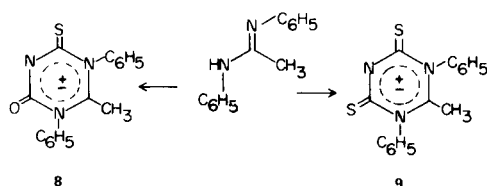
The electron deficiency at the 2-position is evidenced by the reactivity of 2 towards weak nucleophiles such as water and by the deshielding of the 2-position methyl protons of 2a,b. The methyl group resonance of 2a,b occurs at 0.9-1.2 ppm lower field than the methyl group resonances of *N,N'*-diphenyl acetamidine, its cation, or 4a.

Heating 2a with dimethyl acetylenedicarboxylate in refluxing xylene for 20 hours gave the 1:1 adduct 5 instead of 6 or 7 which are analogous to the cycloaddition products expected from the corresponding mesoionic 1,3-disubstituted pyrimidine-4,6-dione (9). Structure assignment for 5 is based upon elemental analysis and spectral evidence



including: vinylic proton signals at δ 5.28, 5.43, and 6.0; carbonyl and carbon-carbon double bond absorption at 1724, 1704, and 1664 cm^{-1} ; and observation of the parent molecular ion in the mass spectrum.

N,N'-Diphenylacetamidine reacted readily in refluxing anhydrous toluene with phenoxy-carbonyl isothiocyanate to give the monothione **8** and with phenoxythiocarbonyl isothiocyanate to give the dithione **9**. Like the *s*-triazine-diones **2**, compounds **8** and **9** were insoluble in most organic solvents, sensitive to moisture, and difficult to purify.



EXPERIMENTAL

Nmr spectra were obtained with a Varian T-60 spectrometer and chemical shifts are reported relative to TMS as an internal standard. Ultraviolet spectra were recorded on a Beckman Model DB spectrophotometer. Infrared spectra were obtained on a Perkin-Elmer Model 237 grating spectrophotometer. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, Georgia. Melting points were determined with a Mel-temp melting point apparatus and are uncorrected. Mass spectra were obtained with a Finnegan Model 1015 quadrupole mass spectrometer using a solid sample direct inlet.

Anhydro-1,3-diphenyl-2-methyl-4-hydroxy-6-oxo-*s*-triazinium Hydroxide (**2a**)

Phenoxy-carbonyl isocyanate (0.9 g., 5.5 mmoles) was added to a solution of *N,N'*-diphenylacetamidine (1.05 g., 5 mmoles) in dry toluene (40 ml.) containing 2 drops of pyridine. After refluxing the reaction mixture for 4 hours under a dry nitrogen atmosphere, the product which had precipitated was collected, washed with dry toluene and dried *in vacuo* to give 1.3 g. (92.9%) of **2a** as white crystals, m.p. 240-242° dec.; ir (potassium bromide): 1730 and 1689 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.18 (s, 3H, CH₃), 7.51 (broad, 10H, aromatic protons); λ max (tetrahydrofuran): 230 nm (ϵ , 9,850); ms (70 eV): *m/e* 279 parent ion.

Anal. Calcd. for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.76; H, 4.71; N, 14.99.

Anhydro-1,3-dibenzyl-2-methyl-4-hydroxy-6-oxo-*s*-triazinium Hydroxide (**2b**)

Compound **2b**, prepared from *N,N'*-dibenzylacetamidine and phenoxy-carbonyl isocyanate by the above procedure, was obtained as white crystals, m.p. 190-192° dec.; ir (potassium bromide): 1725 and 1690 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.2 (s, 3H, CH₃), 5.4 (s, 4H, -CH₂-), 7.4 (s, 10H, aromatic protons); ms (70 eV) *m/e* 307 parent ion.

Anal. Calcd. for C₁₈H₁₇N₃O₂: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.26; H, 5.64; N, 13.62.

Compounds **2c-e** were prepared as described above from the corresponding *N,N'*-disubstituted amidine and exhibited spectral properties consistent with those described. As with **2a,b** attempted

purification by recrystallization from chloroform, dimethylformamide-ether, or other solvents generally gave products with lower melting points and unsatisfactory elemental analyses.

1-Acetyl-1,5-diphenylbiuret (**4a**)

Recrystallization of **2a** from wet chloroform-petroleum ether gave **4a** as white crystals, m.p. 160-162°; ir (potassium bromide): 3100 (N-H), 1718, and 1678 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.0 (s, 3H, CH₃), 7.05-7.81 (m, 10H, aromatic protons), 9.41 (broad s, 1H, -NH-), and 10.65 (broad s, 1H, -NH-); ms (70 eV): *m/e* 297 parent ion. A sample for analysis was recrystallized from chloroform-petroleum ether.

Anal. Calcd. for C₁₆H₁₅N₃O₃: C, 64.64; H, 5.09; N, 14.13. Found: C, 64.95; H, 5.30; N, 14.02.

1,3-Diphenyl-2-methylidene-5-(dimethylethylene-1',2'-dicarboxylate)hexahydro-*s*-triazine-4,6-dione (**5**)

A mixture of **2a** (0.28 g., 1 mmole) and dimethylacetylene dicarboxylate (0.156 g., 1.1 mmoles) in dry xylene (15 ml.) was refluxed for 20 hours. The precipitate which formed on cooling was collected and washed with toluene. Recrystallization from trifluoroacetic acid-ether gave **5** as white crystals, m.p. 211-212°; ir (potassium bromide): 1724, 1704 (C=O), and 1664 cm^{-1} (C=CH₂); nmr (trifluoroacetic acid): δ 4.03 (s, 6H, OCH₃), 5.28 (d, 1H, =CH₂), 5.43 (d, 1H, =CH₂), 6.0 (s, 1H, vinyl proton), 7.23-7.91 (m, 10H, aromatic protons); λ max (ethanol): 244 nm (ϵ , 7,950) and 301 (3,800).

Anal. Calcd. for C₂₂H₁₉N₃O₆: C, 62.70; H, 4.54; N, 9.97. Found: C, 62.90; H, 4.56; N, 9.93.

Anhydro-1,3-diphenyl-2-methyl-4-hydroxy-6-thioxo-*s*-triazinium Hydroxide (**8**)

Phenoxy-carbonyl isothiocyanate (**10**) (1.0 g., 5.5 mmoles) was added to a solution of *N,N'*-diphenylacetamidine (1.05 g., 5 mmoles) in dry toluene (40 ml.) containing 2 drops of pyridine. The reaction mixture was refluxed for 4 hours under a dry nitrogen atmosphere. Upon cooling, the precipitate which had formed was collected, washed with toluene and dried *in vacuo* to give, after recrystallization from DMF, 0.9 g. (61%) of **8** as yellow crystals, m.p. 250-251°; ir (potassium bromide): 1709 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.25 (s, 3H, CH₃), 7.15-7.71 (m, 10H, aromatic protons); λ max (tetrahydrofuran): 266 nm (ϵ , 20,000); ms (70 eV): *m/e* 295 parent ion.

Anal. Calcd. for C₁₆H₁₃N₃SO: C, 64.08; H, 4.44; N, 14.23. Found: C, 64.88; H, 4.53; N, 14.06.

Anhydro-1,3-diphenyl-2-methyl-4-mercapto-6-thioxo-*s*-triazinium Hydroxide (**9**)

A mixture of phenoxythiocarbonyl chloride (0.5 g., 5 mmoles) and lead thiocyanate (0.8 g., 2.5 mmoles) in dry toluene (30 ml.) was refluxed for 2 hours. The precipitated lead chloride was removed by filtration and 2 drops of pyridine added to the filtrate. To this solution was added *N,N'*-diphenylacetamidine (1.05 g., 5 mmoles) and the resulting solution was refluxed for 4 hours. The precipitate which formed upon cooling was collected, washed with dry toluene and dried *in vacuo* to give, after recrystallization from DMF, 0.93 g. (59.8%) of **9** as yellow crystals, m.p. 242-243°; λ max (tetrahydrofuran): 272 nm (ϵ , 32,100) and 295 (24,200); nmr (deuteriochloroform): δ 3.26 (s, 3H, CH₃) and 7.21-7.68 (m, 10H, aromatic protons); ms (70 eV): *m/e* 311 parent ion.

Anal. Calcd. for C₁₆H₁₃N₃S₂: C, 61.73; H, 4.21; N, 13.50; S, 20.56. Found: C, 61.88; H, 4.27; N, 13.42; S, 20.43.

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