

4*H*-Thiopyrans bearing a mesoionic ring

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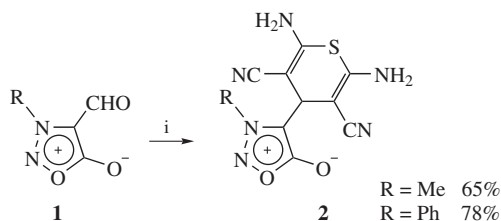
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The preparation of 4-(2,6-diamino-4*H*-thiopyran-3,5-dicarbonitrile) derivatives of sydnone and sydnone imines based on the ternary condensation of 4-formyl sydnones and sydnone imines with malononitrile and 2-cyanothioacetamide is reported.

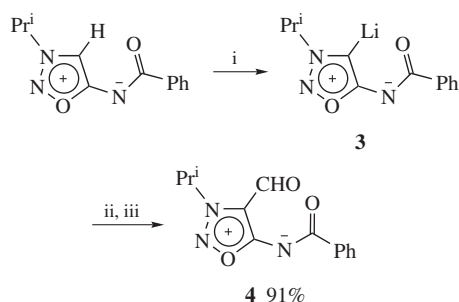
Sydnones (1,2,3-oxadiazolium-5-olates) and their nitrogen analogues, sydnone imines (1,2,3-oxadiazolium-5-amidines), are the mostly investigated representatives of mesoionic heterocyclics and associated with a number of biological activities.^{1–3} Aldehyde functionality at the C(4)-position of these mesoionic heterocycles opens wide perspectives for the construction of numerous promising physiologically active compounds.

Multicomponent condensations involving aryl or heteroaryl carboxaldehydes and malononitrile are widely used in heterocyclic synthesis.^{4,5} However, recent attempts to apply the methodology to 4-formylsydnones **1** failed.⁶ We were the first to discover that the ternary condensation of 3-substituted 4-formylsydnones with malononitrile and 2-cyanothioacetamide affords 2,6-diamino-4-(1,2,3-oxadiazolium-5-olate-4-yl)-4*H*-thiopyran-3,5-dicarbonitriles **2** in good yields (Scheme 1).

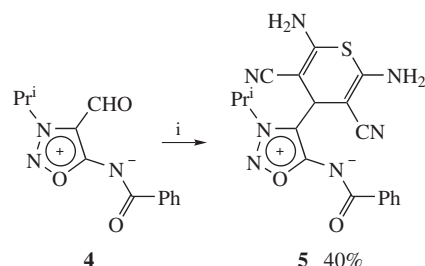


Scheme 1 Reagents and conditions: i, malononitrile (1.0 equiv.), 2-cyanothioacetamide (1.0 equiv.), Et₃N cat., isopropanol, reflux, 0.5 h.

4-Formylsydnone imines were hitherto unknown. Our attempts to prepare these compounds by the Vilsmeier formylation of sydnone imines or by the reaction of 4-lithio derivatives of sydnone imines⁷ with DMF were unsuccessful. However, we found that the interaction of 4-lithio-3-isopropyl-N₆-benzoylsydnone imine **3** with 1-methoxy-*N,N*-dimethylmethanaminium methyl sulfate



Scheme 2 Reagents and conditions: i, BuLi (1.1 equiv.), THF, –85 °C, 0.5 h; ii, 1-methoxy-*N,N*-dimethylmethanaminium methyl sulfate (1.2 equiv.), THF, –85 °C to room temperature; iii, H₂O.



Scheme 3 Reagents and conditions: i, malononitrile (1.0 equiv.), 2-cyanothioacetamide (1.0 equiv.), Et₃N cat., isopropanol, reflux, 0.5 h.

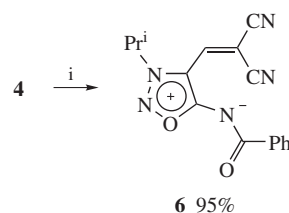
followed by hydrolysis resulted in the corresponding 4-formyl derivatives of sydnone imine **4** in excellent yields (Scheme 2).

We also applied this method to the syntheses of 4-formyl derivatives of sydnones. Thus, for instance, 4-formyl-3-methylsydnone has been obtained in 80% yield by this procedure, while the typical Vilsmeier reaction gives only a 34% yield of the target compound.⁸

The condensation of 4-formylsydnone imine **4** with malononitrile and 2-cyanothioacetamide also leads to 4*H*-thiopyran derivative **5** (Scheme 3). At the same time, the Knoevenagel condensation of **4** with malononitrile almost quantitatively yields methylenemalononitrile derivative **6** (Scheme 4). Compound **6** is an intermediate in the synthesis of thiopyran **5**: a treatment of **6** with 2-cyanothioacetamide also furnished **5** in 93% yield.

The structure of **6** was confirmed by X-ray diffraction analysis (Figure 1).[†] The bond length distribution in **6** is close to expected one for mesoionic molecules.⁹ Due to steric repulsion, the dicyanoethylene moiety is turned off the plane of the mesoionic ring with the torsion angle C(5)C(4)C(15)C(16) of 25.5°. The bond lengths in dicyanoethylene fragment is almost identical to those observed in phenylmethylidenemalononitrile.¹⁰ Thus, we may conclude that the electron-acceptor characteristics of mesoionic cycle are comparable with those of benzene.

The same steric reasons lead to the rather unusual disposition of carbonyl group, which is oriented towards O(1) atom, in



Scheme 4 Reagents and conditions: i, malononitrile (1.0 equiv.), DMAP, AcOH cat., isopropanol, reflux, 0.5 h.

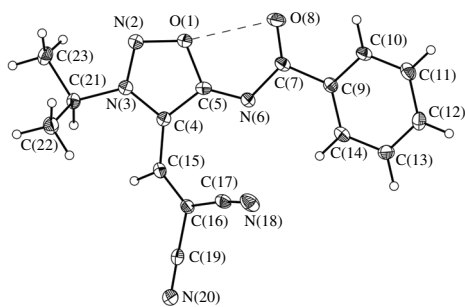


Figure 1 General view of **6** in representation of atoms by thermal ellipsoids ($p = 50\%$). Selected bond lengths (Å): O(1)–N(2) 1.375(2), O(1)–C(5) 1.394(2), N(2)–N(3) 1.293(2), N(3)–C(4) 1.366(2), N(3)–C(21) 1.502(2), C(4)–C(5) 1.416(2), C(4)–C(15) 1.421(2), C(5)–N(6) 1.287(2), N(6)–C(7) 1.391(2), C(7)–O(8) 1.221(2), C(7)–C(9) 1.498(2), C(15)–C(16) 1.352(2).

contrast to acetylsydnone imine picrate¹¹ and *N*-ethoxycarbonyl-3-morpholinosydnone imine dihydrate,¹² in which the *trans* disposition of O(1) and O(8) atoms is observed. Such a mutual disposition of the carbonyl group and mesoionic cycle leads to the occurrence of the shortened contact O(1)⋯O(8) with the interatomic separation of 2.629(1) Å.

In addition to steric repulsion, the conformation of **6** can also be a result of crystal packing effects. Indeed, in a crystal of **6**, one of the CN groups participates in the shortened so-called $N\cdots\pi$ interactions with the mesoionic cycle (see Figure 2). The interaction of this type, rather common for the mesoionic cycle, was also observed in acetonitrile solvate of N_6 -acetyl-3-dimethyl-amino-4-diphenylphosphinosidnonimine palladium dichloride.⁹

In order to analyze the nature of the above shortened contact O(1)⋯O(7), we optimized the geometry of **6** at M052X/6-311++G(d,p) level of theory using the Gaussian03 program.¹³ The geometry of the molecule in the crystal and the gas phase is rather close. In particular, the torsion angle C(5)C(4)C(15)C(16) equal to 29.1 and O(1)⋯O(8) interatomic distances (2.632 Å) are almost the same. The topological analysis of the electron density function $[\rho(r)]$ with the Bader's 'Atom in Molecule' theory¹⁴ in the isolated molecule of **6** has revealed that the

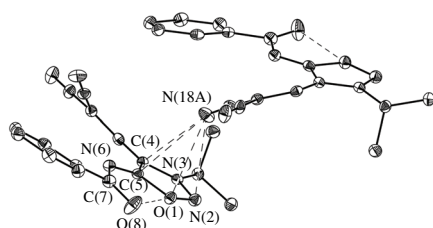


Figure 2 $N\cdots\pi$ interactions in the crystal of **6**. The shortened contacts (Å): N(18A)⋯O(1) 3.047(2), N(18A)⋯N(2) 3.121(2), N(18A)⋯N(3) 3.173(2), N(18A)⋯C(4) 3.164(2), N(18A)⋯C(5) 3.069(2).

[†] *Crystallographic data*: crystals of **6** ($C_{16}H_{13}N_5O_2$, $M = 307.31$) are monoclinic, space group $P2_1/n$, at 100 K: $a = 12.225(2)$, $b = 8.9380(16)$ and $c = 14.159(2)$ Å, $\beta = 103.565(4)^\circ$, $V = 1504.0(4)$ Å³, $Z = 4$ ($Z' = 1$), $d_{\text{calc}} = 1.357$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.94$ cm⁻¹, $F(000) = 640$. Intensities of 8874 reflections were measured with a Smart APEX II CCD diffractometer [$\lambda(\text{MoK}\alpha) = 0.71072$ Å, ω -scans, $2\theta < 58^\circ$] and 3979 independent reflections ($R_{\text{int}} = 0.0386$) were used in further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to $wR_2 = 0.0987$ and $\text{GOF} = 1.001$ for all independent reflections [$R_1 = 0.0452$ was calculated against F for 2828 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using the SHELXTL PLUS 5.0.

CCDC 752298 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

above contact corresponds to bonding interaction – the critical point (3, –1) was located in the interatomic area. Based on the Espinosa correlation scheme,¹⁵ the energy of this contact was found to be 3.7 kcal mol⁻¹. Therefore, the molecular structure of **6** is mostly governed by intra- rather than intermolecular interactions.

Taking into account relatively high decomposition temperature of **6**, this compound can represent a promising material for potential applications in optoelectronics.¹⁶ Therefore, we have estimated its molecular hyperpolarizability (β) at the same level of sophistication as for geometry optimization, which was shown to be accurate enough for calculation of molecular nonlinear optical (NLO) properties.^{17,18} Hyperpolarizability of **6** was estimated by the finite field method as implemented in the Gaussian program (keyword Polar=EnOnly) and presented in a vectorial form according to the expression

$$\beta_{\text{vect}} = \sqrt{\beta_x^2 + \beta_y^2 + \beta_z^2}, \quad \beta_j = \frac{1}{3} \sum_{i=1}^3 (\beta_{jii} + \beta_{iji} + \beta_{ijj}), \quad i, j = x, y, z.$$

The value of β is 934 a.u. and comparable to that of well-known NLO-active compound dicyanovinylanisole (DIVA), which is 1245 a.u. obtained at the same level of theory.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2009.11.008.

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