Sydnone Methides—A Forgotten Class of Mesoionic Compounds for the Generation of Anionic N-Heterocyclic Carbenes

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Abstract: Sydnone methides are described from which only one single example has been mentioned in the literature so far. Their deprotonation gave anions which can be formulated as π-electron rich anionic N-heterocyclic carbenes. Sulfur and selenium adducts were stabilized as their methyl ethers, and mercury, gold as well as rhodium complexes of the sydnone methide carbenes were prepared. Sydnone methide anions also undergo C–C coupling reactions with 1-fluoro-4-iodobenzene under Pd[PPh₃]₄ and CuBr catalysis. ⁷⁷Se NMR resonance frequencies and ¹JC₄ₛₑ coupling constants have been determined to gain knowledge about the electronic properties of the anionic N-heterocyclic carbenes. The carbene carbon atom of the sydnone methide anion 3j resonates at δ = 155.2 ppm in ¹³C NMR spectroscopy at −40°C which is extremely shifted upfield in comparison to classical N-heterocyclic carbenes.

Undoubtedly, sydnones are the best known mesoionic compounds. They are widely applied as masked nitrile imines in 1,3-dipolar cycloadditions (“Huisgen reactions”[11] which proceed in a copper-catalyzed[2] metal-free[3] or metal-free strain-promoted click fashion[4, 5] with sub-millisecond inter- mediates,[6] as summarized in numerous review articles and compilations about[2-3-4]cycloadditions.[7] Recent developments include the synergistic combination of organocatalysis and visible-light photocatalysis of cycloadditions of sydnones and other measures of

Our interest in mesomeric betaines[22] and their relationship to neutral[23, 24] as well as anionic N-heterocyclic carbenes[25] in combination with the introduction of an energy-based quantitative index of the ease of NHC formation from precursors by deprotonation (carbene relative energy of formation, CREF)[26] stimulated initial calculations which suggested that sydnone methides are interesting precursors for the generation of unique π-electron-rich anionic N-heterocyclic carbenes. This index supplements other measures of 0-donor and/or π-properties of NHCs such as molecular electrostatic potentials (MESP), computationally derived ligand electronic parameters (CEP), Tolman parameters (TEP), HOMO energies, calculated proton affinities, JCH and JCSₐ coupling constants of precursor salts and Se adducts, respectively, and Huynh electronic parameters (HEP) of Pd complexes (review[28]). We calculated the CREF value of sydnone methide 2a to be 0.534 (B3LYP/6-311 + + G**) which seemed to be a promising value in comparison to other mesomeric betaines as carbene precursors like 1,3-dimethylimidazolium-4-olate and its 4-amidine, and 1,3-dimethyl-6-oxo-pyrimidinium-4-olate (CREFs = 0.576, 0.557, 0.547, resp.).[24, 25] We therefore report here on the syntheses of a series of sydnone methides, their
conversion into anionic NHCs by deprotonation, and trapping reactions with sulfur, selenium, C-electrophiles, mercury, gold, and rhodium as well as C–C coupling reactions under Pd/Cu-catalysis.

We first developed a reliable synthetic method which lead to a series of sydnone methides 2a–l (Scheme 2, Table 1). Thus, we started from the sydnones 1a–l which we treated with Tf₂O to obtain a mixture of inseparable bis-sydnone ethers and sydnone 5-triflates which proved to be very sensitive towards minute traces of water. Trapping with in situ generated malodinitrile anions for the synthesis of 2b–d, methyl 2-cyanoacetate anions for 2e–h, and 2-(methylsulfonyl)acetonitrile anions for the preparation of 2i–l gave the desired sydnone methides, respectively. These compounds are stable, brilliant yellow to orange in color and slightly fluorescent (see Supporting Information for fluorescence spectroscopy). Sydnone methides can be represented by several resonance structures three of which are shown in Scheme 2. It is interesting to note that carbon atom C4 is a site of negative charge according to the rules of resonance as indicated by mesomeric structure 2a-IB, although it is a site of deprotonation for the formation of anionic N-heterocyclic carbenes. Correspondingly, the C4 carbon atoms resonate at high field between δ = 108.2 ppm (2j) and 110.9 ppm (2f) in 13C NMR spectroscopy. Further DFT calculations predict that the E isomer of 2e is by ΔGiso = 4.6 kJ mol⁻¹ more stable in vacuo than the corresponding Z isomer and that the rotation barrier is ΔEiso = 82.7 kJ mol⁻¹ (PBE0-d3/6-31G**). We also calculated the solvent dependence. In THF, dichloromethane (DCM) and DMSO the rotation barriers decrease to ΔEiso = 65.8 kJ mol⁻¹, ΔEiso = 65.8 kJ mol⁻¹, and ΔEiso = 61.6 kJ mol⁻¹, respectively (see Supporting Information).

These results are in agreement with the fact that the bonds C5–C6 of 2e and 2i [crystallographic numbering, Figure 1] display a considerable double bond character, as determined by single crystal X-ray analyses. As N2 resonates considerably more upfield in 15N NMR spectroscopy than N3, the mesomeric structures 2a-IC can be identified as the most suitable representation for sydnone methides. In the elemental cells, the phenyl ring is twisted by −52.65(17)° (2e) and −12.74(17)° (2i) out of the plane of the sydnone rings. As determined by HMBC measurements, the 1JCH coupling constants of 2a,e,i are 214 Hz, 220 Hz, and 219 Hz, respectively, and these values are between those of 1,3-dimesitylimidazolidinium (1JCH = 225 Hz and 206 Hz) as precursors of normal N-heterocyclic carbenes, respectively, thus indicating strong α-donor capacities of the

![Scheme 2. Syntheses of sydnone methides 2a–l and generation of anionic N-heterocyclic carbenes 3a–l derived thereof (for substitution patterns, see Table 1). Selected mesomeric structures A–C. Several Li species detectable by 7Li NMR due to rapid decomposition of the anions.]

| Compd. | Ar        | Z      | Yield |
|--------|-----------|--------|-------|
| 2a     | Ph        | CN     | 53%   |
| 2b     | 4-C₅H₅Me | CN     | 38%   |
| 2c     | 4-C₅H₅Me | CN     | 28%   |
| 2d     | 4-C₅H₅Cl | CN     | 33%   |
| 2e     | Ph        | COOMe  | 61%   |
| 2f     | 4-C₅H₅Me | COOMe  | 65%   |
| 2g     | 4-C₅H₅Me | COOMe  | 71%   |
| 2h     | 4-C₅H₅Cl | COOMe  | 17%   |
| 2i     | Ph        | SO₂Me  | 63%   |
| 2j     | C₅H₅Me   | SO₂Me  | 37%   |
| 2k     | 4-C₅H₅Me | SO₂Me  | 12%   |
| 2l     | 4-C₅H₅Cl | SO₂Me  | 9%    |

![Figure 1. Molecular drawing of sydnone methide 2e (above) and 2i (below) (displacement parameters are drawn at 30% (2e) and 50% (2i) probability level). Selected bond lengths of 2e [pm] (crystallographic numbering): N3–C4: 134.12(15), C4–C5: 138.91(15), C5–C6: 139.80(15), C6–S7: 172.16(13), C6–S8: 139.87(16), C6–C7: 143.83(17), C7–C8: 121.05(15), C9–N9: 114.51(18) pm. Selected torsion angles of 2e [°]: N2–N3–C13–C18: 128.96(13), C4–C5–C6–C7: −1.8(2) °. Selected bond lengths of 2i [pm]: N3–C4: 135.00(17), C4–C5: 138.10(17), C5–C6: 139.80(18), C6–C7: 172.16(13), C7–O9: 144.04(10), C11–N12: 115.02(18) pm. Selected torsion angles of 2i [°]: N2–N3–C13–C18: −12.74(17), C4–C5–C6–C7: 11.6(2) °.]

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corresponding N-heterocyclic carbenes.[33] We next performed a base screening which revealed that deprotonation of the sydnone methides 2a–l can best be accomplished by LiHMDS in THF at −10°C. According to the rules of resonance, the resulting anions 3a–l can be represented by a number of canonical forms, among those the mesomeric structures of abnormal N-heterocyclic carbenes 3a–IA, as structures possessing two formal negative charges at C4 3a–IB, and as normal anionic N-heterocyclic carbenes 3a–IC (Scheme 2).

Although the anions 3a–l are instable and decompose rapidly even at low temperatures, we successfully generated 3j quantitatively at −50°C and immediately measured NMR spectra at −40°C. The 1H NMR spectra show the absence of the proton at C4. In the 13C NMR spectra the signal of C4 of the precursor shifted considerably from 108.2 ppm (2j) to 155.2 ppm (3j). The carbene’s resonance frequency is thus extremely shifted upfield in comparison to other NHCs. All chemical shift differences are summarized in Table S2 (Supporting Information). Moreover, the mass of the sydnone methide anion 3j was confirmed by high resolution electrospray ionization mass spectrometry in the anion detection mode on spraying a cooled in situ prepared sample of 3j. To gain insight into the electronic properties of the sydnone methide anions we performed DFT calculations (B3LYP/6-311++G**). In contrast to 1,3-dimesitylimidazol-2-ylidene and 1,3-dimesitylimidazolidin-2-ylidene which we chose as examples, the highest occupied molecular orbitals (HOMOs) of the sydnone methide carbenes 3a, 3e and 3l are π-orbitals with significant atomic orbital coefficients on C4 as legacy of the singlet state (Figure 2). The HOMO−1 display the characteristic geometries of N-heterocyclic carbenes. Their energies are considerably higher than those of the aforementioned N-heterocyclic carbenes of imidazole, but slightly lower than those of N-phenylsydnone (Figure 3). Concerning the substituent effects, the different electron-withdrawing capacities of the COOMe group (Hammett constants[6] αp = 0.37; αN = 0.45), CN group (αp = 0.56; αN = 0.66) and SOMe group (αp = 0.60; αN = 0.72) correlates with the HOMO energies within the series of sydnone methide anions.

Reaction of the in situ generated anionic sydnone methide carbenes 3a,e,i with sulfur and selenium gave the thiocarbethioethers 4a–e and selenium ethers 5a–e after methylation as stable compounds, respectively (Scheme 3). The 77Se NMR resonance frequencies of the selenium ethers 5a–e were detected at δ = 86 ppm, 101 ppm and 109 ppm, respectively, and these values correspond to those measured for Molsidomine [that is, N-(ethoxycarbonyl)-3-(4-morpholino)sydnone imine; δ = 97 ppm].[37] As expected they are considerably more upfield than those of the selenium ethers of 1,3-dimesitylimidazol-2-ylidene and its imidazolidine derivative which are cations and which resonate at δ = 199 ppm and 271 ppm, respectively. Treatment of 3a,e,i with acetyl chloride (R = Me) and benzoyl chloride (R = Ph) gave 6a–e which slowly reconstitute the corresponding sydnone methides on exposure to water. The acetyl derivative of 6f (Z = SOMe, R = Me) could not be isolated as it is unstable under ambient conditions. These reactions correspond to rare trapping reactions of normal[34,35] as well as abnormal imidazolidylidenes with acyl chlorides.[36] Mesoionic compounds such as 1,3-dimesitylimidazolium-4-olates, however, undergo electrophilic heteroaromatic substitutions to give these structures.[39]

The reaction of 3e,f with 0.5 equiv of mercury(II)-chloride lead to the predominant formation of the dimeric mercury complexes 7(a,b), whereas 3–4 equiv of HgCl2 yielded the monomeric complexes 7a,b from 3b,f.
Chloro(triphenylphosphine)gold(I) converted the sydnone methide carbenes 3c,f,i into the gold(I) complexes 8a–c as yellow solids (Scheme 4). We also reacted the sydnone methide carbenes 3a,f,i with RhCO(PPh3)Cl which resulted in the formation of the rhodium complexes 9a–c as pale yellow solids.

Single crystals of the gold complex 8a were subjected to an X-ray analysis (Figure 4). The results show that complex formation does not influence the starting mesoion/C29s geometry (2a) significantly.

Concerning C–C coupling reactions, treatment of 3a,e,i with CuBr gave in situ generated, non-isolable copper compounds, which coupled with 4-fluoro-1-iodobenzene in the presence of Pd(PPh3)4 in acceptable yields (Scheme 5). These reactions proceed in analogy to those of sydrones.[41]

In summary, we present the syntheses, spectroscopic characterizations, results of calculations,[42,43] and single crystal X-ray analyses of new stable members of the substance class of sydnone methides from which only one single example had been described in 1984. Deprotonation yielded sydnone methide anions which can be formulated by a number of resonance forms, among those mesomorphic structures of anionic N-heterocyclic carbenes. The frontier orbital profile sets these N-heterocyclic carbenes apart from other examples of this class of compounds, as their highest occupied molecular orbitals are r-orbitals with considerable atomic orbital coefficients on the carbene carbon atom, and extremely upfield shifted13C NMR resonance frequencies of the carbene carbon atom (3j: δ = 155.2 ppm). The sydnone methide anions can be reacted with sulfur and selenium, respectively, and stabilized by S- and Se-methylation. Reaction with acyl chlorides gave sydnone methide ketones, and trapping reactions with mercury, gold, and rhodium gave the corresponding complexes. Finally, we presented a Pd0/CuI-catalyzed C–C coupling reaction at C4 of the sydnone methide. Our results supplement the knowledge about the sydnone family of compounds as well as about anionic N-heterocyclic carbenes.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: betaines · carbenes · heterocycles · rhodium · selenium

Scheme 4. Trapping of the sydnone methide anionic carbenes with as mercury, gold, and rhodium complexes, respectively.

Scheme 5. Copper-catalysed C–C coupling reactions.

X-ray analyses[44,45] of new stable members of the substance class of sydnone methides from which only one single example had been described in 1984. Deprotonation yielded sydnone methide anions which can be formulated by a number of resonance forms, among those mesomeric structures of anionic N-heterocyclic carbenes. The frontier orbital profile sets these N-heterocyclic carbenes apart from other examples of this class of compounds, as their highest occupied molecular orbitals are r-orbitals with considerable atomic orbital coefficients on the carbene carbon atom, and extremely upfield shifted13C NMR resonance frequencies of the carbene carbon atom (3j: δ = 155.2 ppm). The sydnone methide anions can be reacted with sulfur and selenium, respectively, and stabilized by S- and Se-methylation. Reaction with acyl chlorides gave sydnone methide ketones, and trapping reactions with mercury, gold, and rhodium gave the corresponding complexes. Finally, we presented a Pd0/CuI-catalyzed C–C coupling reaction at C4 of the sydnone methide. Our results supplement the knowledge about the sydnone family of compounds as well as about anionic N-heterocyclic carbenes.

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Sydnone Methides—A Forgotten Class of Mesoionic Compounds for the Generation of Anionic N-Heterocyclic Carbenes

Except for a single example, sydnone methides have been unknown to date. Syntheses are described here, leading to 10 stable and intensely colorful, slightly fluorescent sydnone methides with \( Z = \text{CN}, \text{COOMe}, \text{and SO}_2\text{Me}, \) respectively.

On deprotonation, unique anionic \( \pi \)-electron-rich N-heterocyclic carbenes are formed which react to thioethers and selenoethers, mercury, gold and rhodium complexes, and 4-acylsydnone methide on treatment with acyl chlorides.