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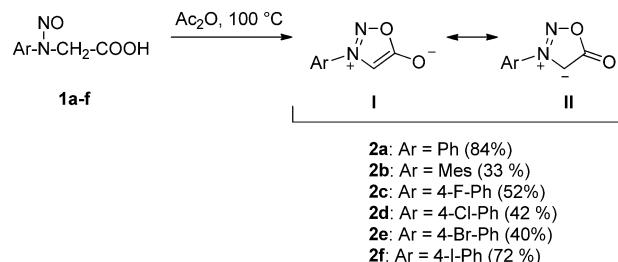
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Deprotonated sydrones, which can be represented as anionic N-heterocyclic carbenes, were prepared as Li adducts and compared with deprotonated O-ethylsydrones (5-ethoxy-1,2,3-oxadiazol-4-ylidenes) which belong to the class of abnormal NHCs. The Pd complexes of the sydnone anions (X-ray analysis) as well as of the O-ethylsydnone carbenes proved to be efficient catalysts in aryl couplings of thiophenes.

Of all the 228 theoretically predicted mesoionic compounds¹ sydrones are probably the most prominent. Sydrones (1,2,3-oxadiazolium-5-olates) are 5-membered representatives of the class of conjugated mesomeric betaines (CMB) which is one of four distinct categories of this class of compounds.² They are not only known as versatile 1,3-dipoles in [2+3]-cycloadditions but also as biologically active compounds.³ So far the chemistry of sydrones has not been associated with the chemistry and applications of N-heterocyclic carbenes which have developed rapidly during the last two decades. Numerous structural variations of N-heterocyclic carbenes have been described, most of them aiming at enhancing the electron density at the carbene center and thus influencing the σ -donor capacity in catalytically active metal complexes.⁴ Recently mesomeric betaines including mesoionic compounds, however, have also come into the focus of carbene research. First results of interconversions of mesomeric betaines into N-heterocyclic carbenes and *vice versa* are summarized in recent review articles.⁵ In continuation of our interest in N-heterocyclic carbenes and mesomeric betaines⁶ we report here on sydrones as well as on O-ethylsydrones (5-ethoxy-1,2,3-oxadiazolium salts) and deprotonated species derived thereof.

We prepared a series of sydrones **2a-f** by cyclization of *N*-nitroso amino acids **1a-f** with acetic anhydride (Scheme 1). Among eight

Sydnone anions and abnormal N-heterocyclic carbenes of O-ethylsydrones. Characterizations, calculations and catalyses[†]

 Sascha Wiechmann,^a Tyll Freese,^a Martin H. H. Drafz,^a Eike G. Hübner,^a Jan C. Namyslo,^a Martin Nieger^b and Andreas Schmidt^{a*}


Scheme 1

dipolar resonance forms of sydrones, **I** is the most common. The best single representation which reflects the properties of sydrones, however, appears to be **II**.⁷ Resonance form **II** is in agreement with carbonyl stretching frequencies of **2a-f** between 1728 cm^{-1} and 1736 cm^{-1} . Bond length (1.197 Å), calculated from IR spectra of **2a**, and bond order (1.99) correspond to an exocyclic C=O double bond which can also be seen in a single crystal X-ray analysis of **2b** (ESI[†]). We calculated the NICS(1)⁸ value of **2a** (−6.8) which is between the cyclopentadienyl anion (−12.3) and cyclopentane (−2) (DFT LACVP*/B3LYP). In summary these values confirm that sydrones are not aromatics.

In contrast to other mesoionic compounds such as nitron³ and imidazolium-4-aminide⁴¹⁰ no hints on tautomeric equilibria between sydrones and their N-heterocyclic carbenes can be found in the spectra. DFT calculations revealed that the mesoionic form **2aA** is considerably more stable than its tautomer **2aB** [$\Delta E = +191 \text{ kJ mol}^{-1}$] (Scheme 2). Except for few photochromic sydrones,¹¹ valence isomers such as **2aC** are not detectable.

A base screening employing LiOtBu, NaOtBu, KOtBu, KH, LiAlH₄ and *n*BuLi in a variety of solvents, respectively, which have been used earlier to deprotonate sydrones for further functionalizations at C4,^{3,7} caused a decomposition of the sydrones **2a-f**, when we tried to isolate the deprotonated species. Fortunately, deprotonation by cyanomethyl lithium, freshly prepared from *n*BuLi and anhydrous MeCN, resulted in the formation of the sydnone anions **5a-f** in quantitative yields

^a Clausthal University of Technology, Institute of Organic Chemistry, Leibnizstrasse 6, D-38678 Clausthal-Zellerfeld, Germany. E-mail: schmidt@ioc.tu-clausthal.de

^b Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, P.O. Box 55 (A.I. Virtasen aukio 1), FIN-00014, Helsinki, Finland

[†] Electronic supplementary information (ESI) available: Crystallographic data of **2b** and *trans*-**16**. CCDC 987516 and 987969. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc05461j

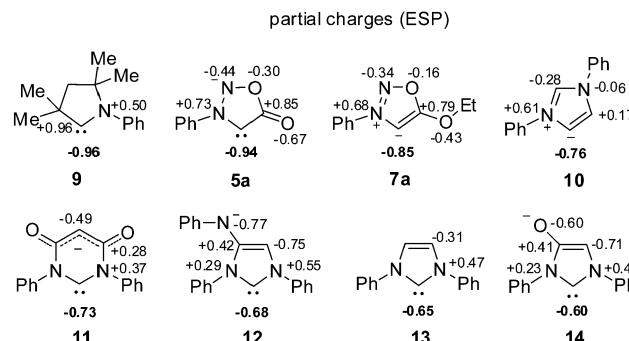
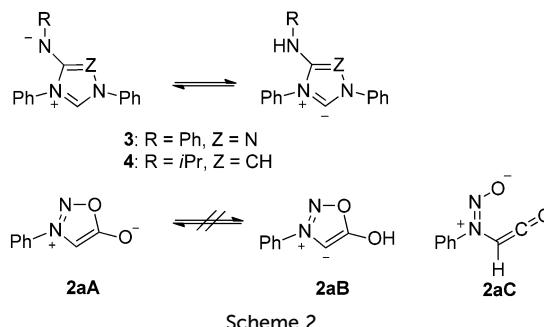
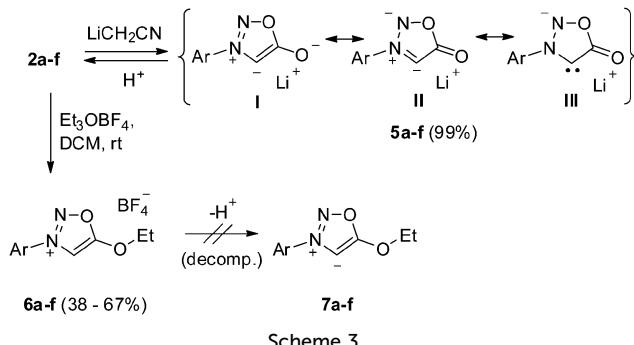


Fig. 1 Calculated partial charges of the title compounds and selected NHCs.



as colorless, moisture-sensitive compounds which proved to be stable under an inert atmosphere for several weeks (Scheme 3). On exposure to water or protic solvents, reprotonation of **5a-f** to the sydnone **2a-f** occurred, which were recovered quantitatively in all cases. Ethylation of the sydnone **2a-f** by triethyloxonium tetrafluoroborate gave the 5-ethoxy-1,2,3-oxadiazolium salts **6a-f** which are stable under an inert atmosphere up to approximately 60 °C. As the calculated NICS(1) value of **6a** is -8.9 these *O*-ethylysdnones are slightly more aromatic than the corresponding sydnone. The isolation of the abnormal N-heterocyclic carbenes (aNHC) **7a-f**, however, failed, as all attempts to deprotonate the *O*-ethylysdnones resulted in decomposition products.

Sydnone anions can be represented by several resonance forms, among those representations as anionic abnormal NHCs **I** and **II**, and the anionic NHC **III**. Do sydnone anions bear more than a formal relationship to N-heterocyclic carbenes? As a matter of fact, the calculated bond lengths of C4–C5 (1.451 Å), C5=O (1.227 Å), and N3–C4 (1.353 Å) are best represented by resonance form **II**. As calculated by us and found IR-spectroscopically,¹² the lithium cation is located between C4 and the exocyclic oxygen of **5a**. By contrast, the aNHC **7a** is best represented as shown, as the calculated C4–C5 bond (1.390 Å) is shortened in comparison to **5a**, whereas the C5–O and O–Et bonds are essentially C_{sp}²–O and O–C_{sp}³ single bonds (1.325 and 1.445 Å, resp.). The ESP partial charges of C4 of the sydnone anion **5a** as well as of the aNHC **7a** adopt values between the CAAC **9**¹³ on the one hand, and the aNHC **10**¹⁴ on the other (Fig. 1). As a comparison, we also calculated the phenyl derivatives of carbene **11**¹⁵ derived from a cross-conjugated mesomeric betaine, the anionic NHCs **12**¹⁶ and **14**¹⁷ derived from the mesoionic compounds imidazolium-4-aminide and

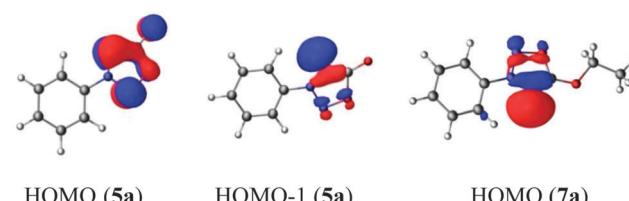


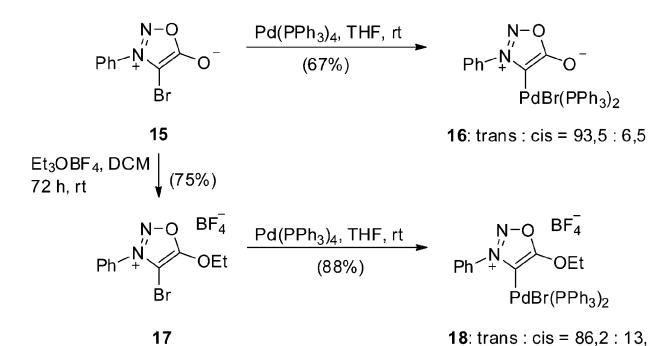
Fig. 2 Calculated highest occupied molecular orbitals.

imidazolium-4-olate, respectively, and the NHC imidazole-2-ylidene **13**. Similar to N-heterocyclic carbenes derived from ylides¹⁸ the calculated HOMO of **5a** is a π -orbital with a large coefficient on C4, whereas the HOMO – 1 is perpendicular to the HOMO and contains the lone pair of electrons at C4 (Fig. 2).

As expected the HOMO of the aNHC **7a** is mainly a σ -type molecular orbital as shown.

Palladium complexes to stabilize the aNHC **7a** and to study catalytic activities were prepared as follows. 4-Bromo-N-phenylsydnone **15** formed the palladium complex **16** of the sydnone anion **5a** as a mixture of *trans* and *cis* isomers (Scheme 4).¹⁹ We were able to perform a single crystal X-ray analysis of *trans*-**16** (ESI \dagger). Ethylation of the bromosydnone **15** under exclusion of moisture resulted in the formation of the new 4-bromo-1,2,3-oxadiazolium salt **17** in good yields, which served as starting material for the preparation of the Pd complex **18** of the aNHC **7a**.

The Pd complexes **16** and **18** of the sydnone anion **5a** as well as the aNHC **7a** proved to be efficient catalysts in Suzuki–Miyaura



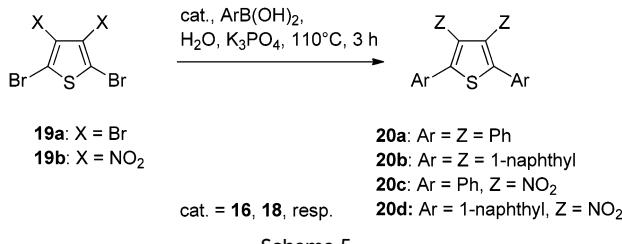


Table 1 Catalysts and yields

Entry	Starting material	Product	Catalyst	Yield ^a (%)
1	19a	20a	16	55
2	19a	20a	18	74
3	19a	20b	16	53
4	19a	20b	18	60
5	19b	20c	16	91
6	19b	20c	18	85
7	19b	20d	16	80
8	19b	20d	18	79

^a Isolated yields.

cross-coupling reactions (Scheme 5). Thus, the perphenylation of tetrabromothiophene **19a** to **20a** proceeds in considerably higher yields and in shorter periods of time under the conditions shown (Table 1, entries 1 and 2) in comparison to the catalyst system Pd(PPh₃)₄/K₃PO₄ (tol, H₂O, 12 h, 90 °C) which gave 37% yield of **20a**.²⁰ The pernaphthylation of **19a** to the hitherto undescribed 2,3,4,5-tetra(naphthalen-1-yl)thiophene **20b** gave 53% and 60% yield, respectively, when the complexes **16** and **18** were employed (entries 3 and 4). The 2,5-bisarylation of 2,5-dibromo-3,4-dinitrothiophene **19b** with phenylboronic acid gave 3,4-dinitro-2,5-diphenylthiophene **20c** in excellent yields under catalysis of **16** and **18**, respectively (entries 5 and 6). Compound **20c** has been prepared before in 37% yield by cross-coupling using Pd(PPh₃)₄, K₂CO₃ in MeOH and toluene over a period of 8 h at reflux temperature.²¹ An alternative procedure uses 1,2-dimethoxyethane as solvent to give 80%, however, after a reaction time of 13 h at reflux temperature.²² Whereas the cross-coupling to 2,5-di(naphthalen-1-yl)-3,4-dinitrothiophene **20d**, which is a new compound, under Pd(PPh₃)₄ catalysis proceeded in only 40% yield, catalysis by **16** or **18** gave very good yields (entries 7 and 8).

Syndnone anions share typical features with N-heterocyclic carbenes, and their deprotonated *O*-ethyl derivatives, 5-ethoxy-1,3,4-oxadiazol-4-ylidene, belong to the class of abnormal NHCs. Either species form stable Pd complexes which are efficient catalysts in Suzuki–Miyaura cross-coupling reactions.

Notes and references

- W. D. Ollis and C. A. Ramsden, *Adv. Heterocycl. Chem.*, 1976, **19**, 1; C. A. Ramsden, in *Comprehensive Organic Chemistry*, ed. P. G. Sammes (Hrsg.), Pergamon Press, Oxford, 1979, vol. 4, p. 1171.
- W. D. Ollis, S. P. Stanforth and C. A. Ramsden, *Tetrahedron*, 1985, **41**, 2239.

- D. L. Browne and J. P. Harrity, *Tetrahedron*, 2010, **66**, 553; T. L. Gilchrist, *Sci. Synth.*, 2004, **13**, 109; R. Chandrasekhar and M. J. Nanjan, *Mini-Rev. Med. Chem.*, 2012, **12**, 1359.
- Selected publications: M. N. Hopkinson, C. Richter, M. Schedler and F. Glorius, *Nature*, 2014, **510**, 485; J. C. Bernhammer, N.-X. Chong, R. Jothibusu, B. Zhou and H. V. Huynh, *Organometallics*, 2014, **33**, 3607; Q. W. Zhao, D. P. Curran, M. Malacria, L. Fensterbank, J. P. Goddard and E. Lacôte, *Chem. – Eur. J.*, 2011, **17**, 9911; J. A. Mata and M. Poyatos, *Curr. Org. Chem.*, 2011, **15**, 3309; *N-Heterocyclic carbenes, from laboratory curiosities to efficient synthetic tools*, ed. S. Díez-González, Royal Society of Chemistry Publishing, Cambridge, 2011; T. Dröge and F. Glorius, *Angew. Chem. Int. Ed.*, 2010, **49**, 6940; G. Guisado-Barrios, J. Bouffard, B. Donnadieu and G. Bertrand, *Angew. Chem. Int. Ed.*, 2010, **49**, 4759; A. Schmidt, A. Beutler, M. Albrecht and F. J. Ramírez, *Org. Biomol. Chem.*, 2008, **6**, 287; F. E. Hahn and M. C. Jahnke, *Angew. Chem. Int. Ed.*, 2008, **47**, 3122; D. Holschumacher, T. Bannenberg, C. G. Hrib, P. G. Jones and M. Tamm, *Angew. Chem. Int. Ed.*, 2008, **47**, 7428; V. Lavallo, Y. Canac, B. Donnadieu, W. W. Schöller and G. Bertrand, *Angew. Chem. Int. Ed.*, 2006, **45**, 3488; A. J. Arduengo III, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361.
- A. Schmidt, S. Wiechmann and T. Freese, *ARKIVOC*, 2013, **i**, 424; A. Schmidt and Z. Guan, *Synthesis*, 2012, 3251; A. Schmidt and A. Dreger, *Curr. Org. Chem.*, 2011, **15**, 2897; A. Schmidt and A. Dreger, *Curr. Org. Chem.*, 2011, **15**, 1423; A. Schmidt, A. Beutler and B. Snovsky, *Eur. J. Org. Chem.*, 2008, 4073.
- Selected publications: Z. Guan, S. Wiechmann, M. Drafz, E. Hübner and A. Schmidt, *Org. Biomol. Chem.*, 2013, **11**, 3558; A. Schmidt and A. Rahimi, *Chem. Commun.*, 2010, **46**, 2995; A. Schmidt, N. Münster and A. Dreger, *Angew. Chem. Int. Ed.*, 2010, **49**, 2790; A. Schmidt and B. Snovsky, *Synthesis*, 2008, 2798; A. Schmidt and T. Mordhorst, *Synthesis*, 2005, 781.
- T. L. Gilchrist and P. M. O'Neill, *Comprehensive Heterocycl. Chem. II*, 1996, p. 165.
- M. Zora and I. Özkan, *THEOCHEM*, 2003, **638**, 157.
- C. Färber, M. Leibold, C. Bruhn, M. Maurer and U. Siemeling, *Chem. Commun.*, 2012, **48**, 227.
- V. César, J.-C. Tourneux, N. Vujkovic, R. Brousses, N. Lughan and G. Lavigne, *Chem. Commun.*, 2012, **48**, 2349; A. A. Danopoulos, K. Yu. Monakhov and P. Braunstein, *Chem. – Eur. J.*, 2013, **19**, 450.
- S. Nešpůrek, J. Lukáš, S. Böhm and Z. Bastl, *J. Photochem. Photobiol. A*, 1994, **84**, 257; S. Nešpůrek, S. Böhm and J. Kuthan, *THEOCHEM*, 1986, **136**, 261.
- M. G. Ezernitskaya, B. V. Lokshin, E. I. Kazimirchuk, V. N. Khandozhko and V. N. Kalinin, *Mikrochim. Acta, Suppl.*, 1997, **14**, 381.
- V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu and G. Bertrand, *Angew. Chem. Int. Ed.*, 2005, **44**, 5705.
- R. Tonner, G. Heydenreich and G. Frenking, *ChemPhysChem*, 2008, **9**, 1474.
- G. Lavigne, V. César and N. Lughan, *Chem. – Eur. J.*, 2010, **16**, 11432; V. César, N. Lughan and G. Lavigne, *J. Am. Chem. Soc.*, 2008, **130**, 11286.
- A. A. Danopoulos and P. Braunstein, *Chem. Commun.*, 2014, **50**, 3055.
- L. Benhamou, N. Vujkovic, V. César, H. Gornitzka, N. Lughan and G. Lavigne, *Organometallics*, 2010, **29**, 2616; L. Benhamou, V. César, H. Gornitzka, N. Lughan and G. Lavigne, *Chem. Commun.*, 2009, 4720; A. T. Biju, K. Hirano, R. Fröhlich and F. Glorius, *Chem. – Asian J.*, 2009, **4**, 1786.
- N. Pidlypnyi, J. C. Namyslo, M. H. H. Drafz, M. Nieger and A. Schmidt, *J. Org. Chem.*, 2013, **78**, 1070.
- Some Pd complexes have been described before: V. N. Kalinin, F. M. She, V. N. Khandozhko and P. V. Petrovskii, *Russ. Chem. Bull.*, 2001, **50**, 525; V. Kalinin, S. Fan Min and P. Petrovskii, *J. Organomet. Chem.*, 1989, **379**, 195.
- T. T. Dang, N. Rasool, T. T. Dang, H. Reinke and P. Langer, *Tetrahedron Lett.*, 2007, **48**, 845.
- Q. Li, J. Li, R. Yang, L. Deng, Z. Gao and D. Liu, *Dyes Pigm.*, 2012, **92**, 674.
- H. Cheng, B. Djukic, H. A. Jenkins, S. I. Gorelsky and M. T. Lemaire, *Can. J. Chem.*, 2010, **88**, 954.

