An effective synthesis of 4-alkynyl-substituted sydnones

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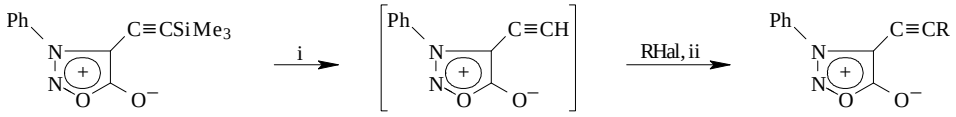
3-Phenyl-4-trimethylsilylethynylsydnone has been obtained for the first time, and a preparative method for the exchange of a Me_3Si group by an organic substrate from organohalides in the presence of Pd^0/Cu^I, Et_3N and $Bu^n_4NF{\cdot}3H_2O$ is proposed.

Mesoionic heterocycles, especially sydnones and sydnone imines, are of considerable interest as potentially physiologically-active compounds.[1] The additional introduction of carbo- and/or heterocyclic substituents into sydnones can have a great impact on their biological activity. Previously we have found that 4-cuprio-3-phenylsydnone reacts with organohalides in the presence of Pd^0 to give cross-coupling products including 4-alkynyl-substituted sydnones.[2,3]

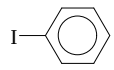
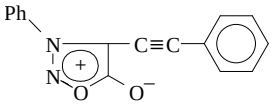
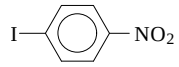
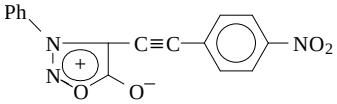
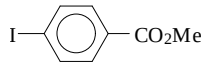
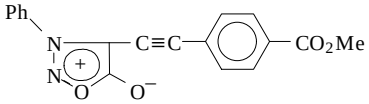
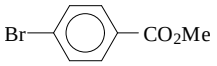
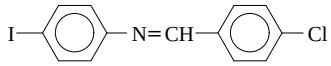
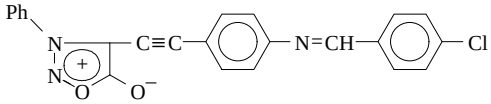
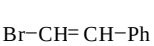
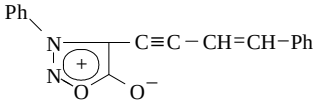
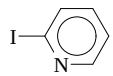
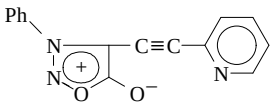
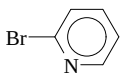
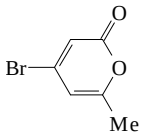
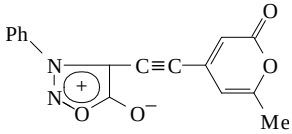
In this work we tried to obtain 4-ethynyl-3-phenylsydnone **1**, because this compound is usable as a base for the synthesis of different 4-carbo- and 4-heterocyclic derivatives of sydnones by cycloaddition [3+2] and [4+2] reactions.[4,5] However, our attempts to synthesize **1** from reactions of 1-bromoacetylene with 4-cuprio-3-phenylsydnone under Pd^0 or Pd^{II} catalysis conditions have not been successful. This may be due to the rather high acidity of the CH bond in terminal acetylenes.

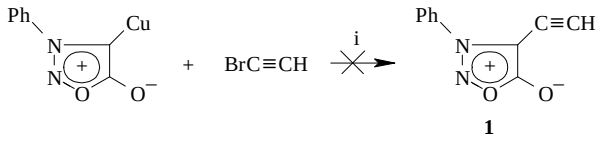
In this respect, to obtain **1** we have used 1-bromo-2-trimethylsilylacetylene[6] as the acetylenic compound for the cross-coupling reaction, because it is known that the silicon–carbon bond in acetylenes is easily cleaved by fluorine anion.[7]

Table 1 Palladium-catalysed cross-coupling reaction of 4-ethynyl-3-phenylsydnone (**1**, *in situ*) with organohalides.

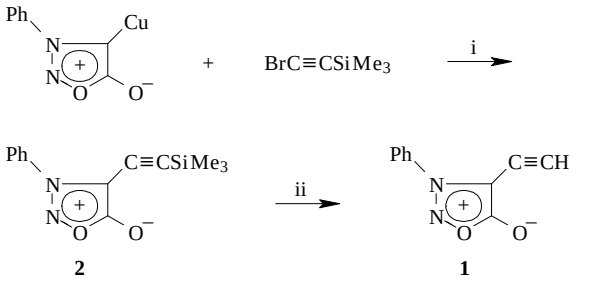


Reagents and conditions: i, $Bu^n_4NF{\cdot}3H_2O$, THF, 20 °C; ii, 5% $Pd(PPh_3)_4$/5% CuI, 4 equiv. Et_3N, THF, 20 °C, 2–24 h.

	RHal	Reaction time/h	Product	Mp/°C	Yield (%)
1		3		133–135 (Lit. data 135.5–137)[3]	85
2		2		159–161	97
3		5		150–152	67
4		24			0
5		5		141–143	49
6		22		112.5–114	40
7		24		123–125	26
8		24			0
9		3		148–150	47



Scheme 1 *Reagents and conditions*: i, $Pd(PPh_3)_4$, THF, 20–60 °C.



Scheme 2 *Reagents and conditions*: i, 5% $Pd(PPh_3)_4$, THF, 20 °C; ii, $Bu^n_4NF{\cdot}3H_2O$.

It has been found that the interaction of 4-cuprio-3-phenylsydnone with 1-bromo-2-trimethylsilylacetylene under Pd^0 catalysis readily results in the formation of the desired 3-phenyl-4-trimethylsilylethynylsydnone – (5-oxido-3-phenyl-4-trimethylsilylethynyl-1,2,3-oxadiazol-3-ium) **2**.†

Treatment of **2** with $Bu^n_4NF{\cdot}3H_2O$ in THF at 0 °C promotes rapid cleavage of the C–$SiMe_3$ bond and the formation of **1** (HPLC data), but all our attemps to prepare **1** in pure form failed due to its instability.

Terminal acetylenes react with organohalides under Pd^0/Cu^I catalysis and in the presence of bases to afford cross-coupling products.[8,9] Compound **1** formed *in situ* from **2** under the action of $Bu^n_4NF{\cdot}3H_2O$ also readily engages in this cross-coupling reaction with vinyl-, aryl- and heteroaryl-halides to give 1-substituted-2-(3-phenylsydnon-4-yl)acetylenes. The main results are presented in Table 1.‡

From Table 1, the palladium-catalysed cross-coupling reaction of **1** with iodoaryls occurs rather fast and in good yields (runs 1–3,5) whereas bromoaryls (runs 4,8) hardly react at all. Bromovinyl (run 6), 2-iodopyrydine (run 7) and 4-bromo-6-methyl-2*H*-pyran-2-one (run 9) form cross-coupling products in moderate yield.

In conclusion, the cross-coupling reactions proposed here are useful as preparative methods for obtaining disubstituted acetylenes where one substituent is a sydnonyl radical.

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References

1 M. Ohta and H. Kato, *Non-Benzenoid Aromatics*, ed. J. P. Snyder, Academic Press, New York, 1969, p. 117.
2 V. N. Kalinin and Fan Min She, *J. Organomet. Chem.*, 1988, **352**, C34.
3 V. N. Kalinin, D. N. Pashchenko and Fan Min She, *Mendeleev Commun.*, 1992, 60.
4 A. S. Onishenko, *Dienovyi Sintez* (*The synthesis of dienes*), Izd. Akad. Nauk SSSR, Moscow, 1963 (in Russian).
5 1,3-*Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley–Interscience, New York, 1984.
6 J. Miller, *Synthesis*, 1983, 128.
7 W. P. Weber, *Silicon Reagents for Organic Synthesis*, Springer–Verlag, New York, 1983.
8 V. N. Kalinin, *Synthesis*, 1992, 413.
9 R. Rossi, A. Carpita and F. Belina, *Organic Preparation and Procedures Int.*, 1995, **27**, 127.

† 5-*Oxido*-3-*phenyl*-4-*trimethylsilylethynyl*-1,2,3-*oxadiazo*-3-*ium* **2**: mp 74.5–76.5 °C. Found (%): C 60.45, H 5.46, N 10.38. Calc. (%) for $C_{13}H_{14}N_2O_2Si$: C 60.44, H 5.46, N 10.48. ^{1}H NMR (δ, ppm, $CDCl_3$): 0.20 (s, 9H, $SiMe_3$), 7.50–7.70 (m, 3H) and 7.75–7.80 (m, 2H, Ph). IR (ν/cm^{-1}, $CHCl_3$): 1764 (CO), 1252 and 848 ($SiMe_3$).

‡ *Typical procedure*: A solution of $Bu^n_4NF{\cdot}3H_2O$ (1 mmol) in 15 ml of THF was added dropwise to a stirred mixture of 3-phenyl-4-trimethylsilylethynylsydnone (1 mmol), organohalide (3 mmol), CuI (0.05 mmol), $Pd(PPh_3)_4$ (0.05 mmol) and Et_3N (4 mmol) in 20 ml of THF. The mixture was stirred 2–24 h (see Table 1) at 20 °C. The solvent was evaporated *in vacuo*, and the product purified by chromatography on silica (eluent $CHCl_3$) and recrystallisation from $CHCl_3$–hexane (3 : 1). All compounds synthesized gave satisfactory analytical and spectroscopic data.

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