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Palladium-catalysed Synthesis of 4-Heteroaryl and 4-Alkynyl-substituted Sydnones. 5-Oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylzinc Chloride

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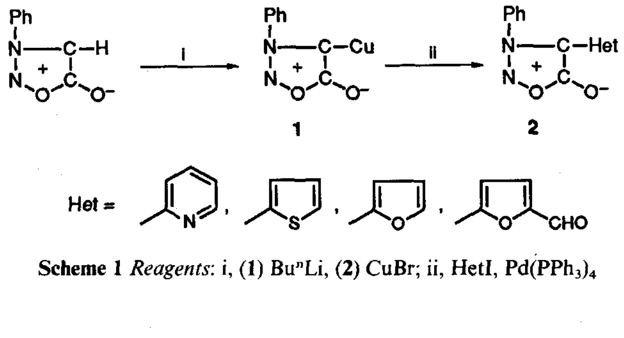
A general method is suggested for the synthesis of 4-heteroaryl- and 4-alkynyl-3-phenyl sydnones by palladium(0)-catalysed cross-coupling of 5-oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylcopper with heteroaryl iodides and alkynyl bromides; 5-oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylzinc chloride has been synthesised and its reactivity investigated.

Mesoionic heterocyclic compounds are of considerable interest as potentially physiologically active compounds.[1] The most readily available examples of such compounds are sydnones and iminosydnones. However, the lack of appropriate methods of introducing different functional substituents into the 4-position of the sydnone nucleus severely restricts their synthetic potential.

Pd-catalysed cross-coupling reactions have been shown to have wide applications in the functionalization of heterocycles.[2] Previously, 5-oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylcopper species, *e.g.* **1**, have been found to react with alkenyl and aryl halides in the presence of $Pd(PPh_3)_4$ to give 4-alkenyl- and 4-aryl-3-phenyl sydnones.[3]

We have found that the Pd-catalysed cross-coupling reaction of compound **1**, obtained *in situ*, with iodoheterocycles can be used as a preparative method for the synthesis of 4-heteroaryl-substituted sydnones **2**. We carried out these reactions with N, O and S-containing iodoheterocycles: 2-iodopyridine, 2-iodofuran, 2-iodothiophene and 5-iodofurfural (Scheme 1).†



Scheme 1 *Reagents*: i, (**1**) Bu^nLi, (**2**) CuBr; ii, HetI, $Pd(PPh_3)_4$

Compound **1** reacted easily with alkynyl bromides in the presence of $Pd(PPh_3)_4$ to yield 4-alkynyl sydnones **3** (Scheme 2). The structures of these compounds have been characterized by NMR, IR, MS and analytical methods (Table 1).

We also synthesized 5-oxido-3-phenyl-1,2,3-oxadiozol-3-ium-4-ylzinc chloride **4**, which was more stable than 4-lithium-substituted sydnone. The former was obtained by transmetallation of the lithium analogue by $ZnCl_2$. Compound **4** was used in Pd-catalysed cross-coupling reactions with alkenyl, alkynyl,

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† *Typical procedure*: A 1.3 mol dm^{-3} solution of Bu^nLi (1.07 ml, 1.2 mmol) in benzene was added dropwise at −78 °C to a stirred solution of 3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (0.2 g, 1.2 mmol) in tetrahydrofuran (THF) (20 ml). The mixture was stirred for 10 min, and then CuBr (0.17 g, 1.2 mmol) [or 0.16 g (1.2 mmol) $ZnCl_2$ for preparation of zinc derivatives] was added. After the mixture had been kept at room temperature for 15 min, $Pd(PPh_3)_4$ (0.07 g, 0.06 mmol) and then heteroaryl (alkynyl) halides (1.2 mmol) were added. After stirring for 2–36 h (depending on the halide), the solvent was evaporated off *in vacuo*, and the residue was separated by column chromatography on silica gel ($CHCl_3$).

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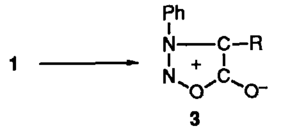
Table 1 Products of palladium-catalysed cross-coupling reaction of 5-oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylcopper and 5-oxido-3-phenyl-1,2,3-oxadiazol-3-ium-4-ylzinc chloride

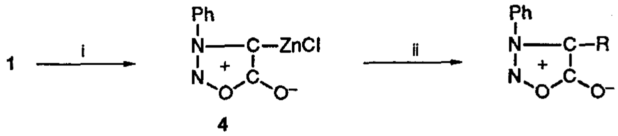
R	M.p./°C	Yield (%)		^{1}H NMR, δ	IR, ν_{CO}/cm^{-1}
		Cu	ZnCl		
Ph	190–192	90^a	27	7.70–7.36 (m, 10H)	1740
p-$C_6H_4NO_2$	168–170	92^a	98	8.13 (d, 2H), 7.80–7.52 (m, 5H), 7.47 (d, 2H)	1735
CH═CHPh (*E*+*Z*)		86^a	86		
C≡CPh	135.5–137	71	3	7.22–7.42 (m, 5H), 7.60–7.83 (m, 5H), 7.84–7.87 (m, 2H)	1752
C≡CC_5H_{11}	Oil	83		0.88 (t, 3H), 1.27 (s, 4H), 1.38–1.47 (m, 2H), 2.41 (t, 2H), 7.59–7.88 (m, 5H)	1754
C≡C$C_{10}H_{21}$	Oil	42		0.87 (t, 3H), 1.23 (s, 14H), 1.25–1.50 (m, 2H), 2.40 (t, 2H), 7.59–7.80 (m, 5H)	1756
2-Pyridyl	122–124	85		7.02–7.09 (m, 1H), 7.40–7.71 (m, 6H), 7.97–8.01 (m, 1H), 8.16–8.19 (m, 1H)	1738
2-Thienyl	176–177.5	98	10	6.98 (m, 1H), 7.25 (m, 2H), 7.43–7.89 (m, 5H)	1732
2-Furyl	119–120.5	80		6.42 (m, 1H), 6.79 (m, 1H), 7.24 (m, 1H), 7.54 (m, 1H), 7.54–7.64 (m, 5H)	1736
5-Furfuryl	143.5–144.5	51	2	7.04 (d, 1H, J_{AB} 4.9 Hz), 7.24 (d, 1H, J_{AB} 4.9 Hz), 7.60–7.55 (m, 5H), 9.37 (s, 1H)	1762 1678^a

^{a} Ref. 3. ^{b} Stretching bands of furfuryl carbonyl group.



R = C≡CC_5H_{11}, C≡C$C_{10}H_{21}$, C≡CPh

Scheme 2 *Reagents*: RBr, Pd(PPh_3)$_4$



R = $C_6H_4NO_2$-*p*, X = I[3]
R = PhCH═CH, X = Br[3]

Scheme 3 *Reagents*: i, (**1**) Bu^{n}Li, (**2**) $ZnCl_2$; ii, RX, Pd(PPh_3)$_4$

aryl and heteroaryl halides but good results were obtained only in reactions with *p*-iodonitrobenzene and β-bromostyrene in the presence of Pd(PPh_3)$_4$ (Scheme 3).

The reactions of **4** with heteroaryl iodides and alkynyl bromides are not interesting for preparative synthesis. It should be noted that the reaction proceeds faster in the case of the copper derivatives (1–3 h) than in the case of the zinc ones (24–72 h). Our attempts to use $PdCl_2$(PPh_3)$_2$ and PhPdI(PPh_3)$_2$ in the reactions mentioned failed.

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References

1 M. Ohta and H. Kato, *Nonbenzenoid Aromatics*, ed. J. P. Snyder, Academic Press, New York, 1969, p. 117.
2 V. N. Kalinin, *Usp. Khim.*, 1991, **60**, 339 (*Russ. Chem. Rev.*, 1991, **60**, 173).
3 V. N. Kalinin and Fan Min She, *J. Organomet. Chem.*, 1988, **352**, C34.