Functionalised Sydnones Through a Facile Metallation of 3-Methyl-4-Phenylsydnone

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Abstract: A metallation reaction of the C-H bond in the methyl group of 3-methyl-4-phenylsydnone has been found to proceed on the action of n-buthyllithium. Subsequent reactions of 3-lithiomethyl-4-phenyl-sydnone thus obtained with electrophiles provide a convenient method for preparation of functionalised sydnones.

Sydnones are unique representatives of mesoionic heterocycles and exhibit a large charge density distribution.¹ The charge distribution at the carbons, nitrogens and oxygens of a number of sydnones were calculated using a PM3 calculation package.² The high positive charge at N3 causes the sydnone ring to behave as an electron withdrawing group. There are no data concerning features of α -CH bonds of acyclic substituents at position 3 of sydnone. We proposed that a strong electron-withdrawing effect of the sydnon-3-yl group would result in activation of C-H bonds in the substituent at N3.

For the first time it has been found that readily available 3-methyl-4-phenylsydnone³ **1** can be easily metallated at the methyl group on the action of n-butyllithium in THF solution at -90° C to give 3-lithiomethyl species **2**. **2** is a rather unstable compound which exists below -90° C for some minutes and undergoes decomposition at elevated temperature. Nevertheless 3-lithiomethyl-4-phenylsydnone **2** reacts readily with a number of electrophiles to form the coupling products⁴ (Scheme, Table).



Scheme. a) n-BuLi, THF, -90 °C, 5min; b) $BrCH_2CH=CH_2$; c) $ClCO_2CH_3$; d) $(CH_3)_3SiCl, e) CO_2$ (solid), then H⁺; f) *p*-ClC₆H₄CHO, then H⁺; g) CH₃COPh, then H⁺; h) PhCOPh, then H⁺

The reactions of 2 with allyl bromide, methyl chloroformate or trimethylsilyl chloride at low temperature afford 3-(but-1'-en-4'-yl)-4-phenylsydnone 3, 3-carbmethoxymethyl-4-phenylsydnone 4 and 3-

Table. Synthesis of the sydnone derivatives from 2				
Entry	Electrophile	Product*	Yield(%)	M.p.(°C)
1	// Br	3	67	56-57
2	CICO ₂ CH ₃ .	4	21	121-122
3	(CH ₃) ₃ SiCl .	5	36	79-80
4	CO ₂ .	6	70	194-196(dec.)
5	сі————————————————————————————————————	7	80	116-118
6		8	12	115-116
7		9	70	195-196

*All compounds synthesized gave satisfactory analytical and spectroscopic data

(trimethylsilyl)methyl-4-phenylsydnone **5** respectively. **2** reacts with carbon dioxide resulting in 3-carboxymethyl-4-phenylsydnone **6**.

It is of importance that **2** can add to carbonyl group of *p*-chlorobenzaldehyde, acetophenone and benzophenone to give corresponding alcohols **7-9**.

In conclusion, the metallation reaction of α -CH bond of alkyl substituent at position 3 of sydnones opens up wide possibilities for obtaining new interesting compounds possessing biological activity.

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References and Notes

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- (2) Tien H.-J.; Lin S.-T.; Sheu J.-T. Can. J. Chem. 1994, 72, 1610.
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- (4) A typical procedure is as follows: To a stirred solution of **1** (500 mg, 2.86 mmol) in dry THF (50 ml) in flame dried flask under nitrogen at -90°C was added n-butyl lithium in hexane (2.86 ml, 1.0N, 2.86 mmol) and the mixture was stirred for 10 min at -90°C. After 5 min a solution of corresponding electrophile (3.43 mmol) in THF (10 ml) was added at -90°C and the mixture was allowed to warm up to room temperature. After an acidification of the mixture with 10% aqueous HCl (1 ml), the solvent was evaporated in vacuo and the residue was purified by chromotography on SiO₂ (eluent ethyl acetate) afford the coupling product.

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