A Simple, Versatile Preparation of Highly Substituted 2,5-Dihydro-oxoles

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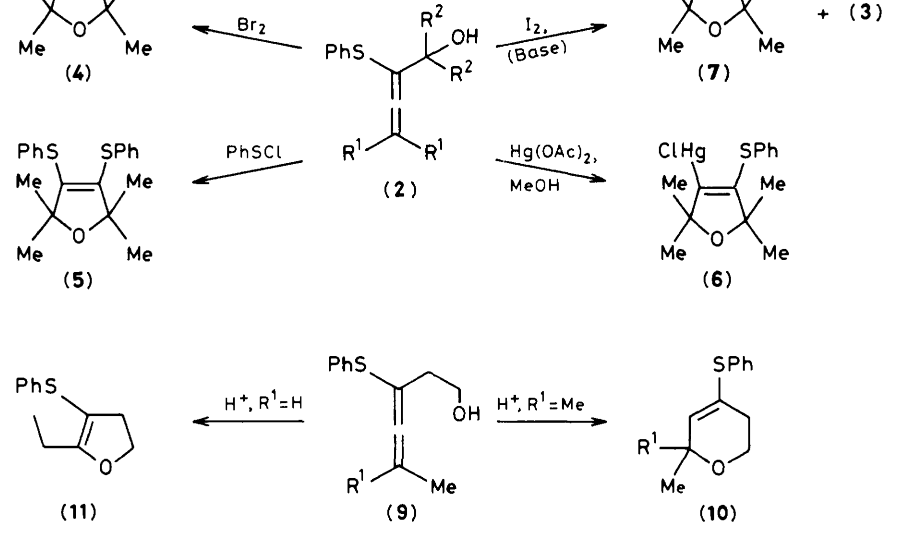
3,3-Dialkyl-1-lithio-1-(phenylthio)allenes (**1**) add efficiently to ketones only on warming to −20 °C or above; the adducts are readily cyclised by acid, or several other electrophiles, to produce highly substituted 2,5-dihydro-oxoles.

We have reported previously[1] that the allenyl-lithium (**1**, R^1 = H) is useful in the preparation of α-phenylthioenones. Initial attempts to extend this preparation, to other than methyl ketones, by use of 3,3-dialkylallenyl-lithiums[2] (**1**, R^1 = alkyl), were only partially successful since the yields of the ketone adducts (**2**, R^1, R^2 = alkyl) were poor (20—30%). Since large proportions of both the quenched allenyl-lithium and ketone were recovered unchanged, even after prolonged reaction times, it was evident that competitive enolisation was the problem. Removing hexamethylphosphoric triamide (HMPA) from the reaction mixture, to slow down proton transfer, did not help, nor did lowering the reaction temperature to −120 °C.[3] However, when the ketone was added to the allenyl-lithium at −20 or 0 °C in tetrahydrofuran (THF) yields improved dramatically, and the adducts (**2**) shown in Table 1 were obtained in 43—81% purified yields. Despite the absence of HMPA,[1] there was very little if any of the unwanted homoprop-2-ynylic (γ-alkylation) products.

The adducts (**2**) proved to be very reactive towards electrophiles. In aprotic media, traces of trifluoroacetic acid



Reactions giving (**4**)—(**7**) are for (**2**, R^1 = R^2 = Me).

Table 1. [a] Formation of adduct (**2**) and dihydro-oxole (**3**) from allene (**1**).

			% Yield	
Entry	R^1	R^2	(**2**)	(**3**) (crude)
1	Me	Me	81	79 (100)
2	Me	$-[CH_2]_5-$	78	46 (100)
3	Me	$-[CH_2]_4-$	65	42 (93)
4	$-[CH_2]_5-$	Me	43	41 (88)
5	$-[CH_2]_5-$	$-[CH_2]_5-$	51	74 (91)
6	$-[CH_2]_5-$	$-[CH_2]_4-$	44	56 (84)

[a] All new compounds were fully characterized. Yields, except those in parentheses, are for isolated, purified materials.

led to rapid cyclisation[4] to the 2,5-dihydro-oxole (**3**) in near-quantitative crude yields, which, along with the purified yields, are quoted in Table 1. The use of an exocyclic allene or a cyclic ketone in this sequence led readily to spirodihydro-oxoles (*e.g.*, entries 2, 3, and 4), and combination of both gave bis-spirodihydro-oxoles (entries 5 and 6).

We also investigated the cyclisation of the alcohol (**2**, $R^1 = R^2 =$ Me) with some other electrophiles. Addition of Br_2[5] in CH_2Cl_2 at 25 °C led to immediate reaction and isolation of the bromo-derivative (**4**) in 93% crude yield,[6] whilst addition of PhSCl[7] gave the bis(phenylthio)-compound (**5**) in 72% yield. The alcohol (**2**, $R^1 = R^2 =$ Me) was also cyclised by mercury(II) acetate in methanol,[8] to give the mercuriochloride (**6**) in 32% yield, presumably obtained by facile ligand exchange during a brine wash.

The reaction between the alcohol (**2**, $R^1 = R^2 =$ Me) and I_2 was very complex. I_2 in CH_2Cl_2 produced the 4-unsubstituted compound (**3**; $R^1 = R^2 =$ Me) only, but, in polar solvents (H_2O, MeOH, or *N,N*-dimethylformamide) containing mild bases (NEt_3, pyridine, or K_2CO_3), the reaction with I_2 gave 40—60% yields of mixtures of (**3**) and the iodo-compound (**7**), in ratios which varied from 2:1 to 1:4. Even use of large excesses of I_2 and/or base did not suppress the formation of (**3**) efficiently.

The dihydro-oxole (**3**, $R^1 = R^2 =$ Me) underwent substitution reactions with Br_2 and with PhSCl, giving good yields of the bromide (**4**) and the sulphide (**5**) respectively, but it did not react with either $Hg(OAc)_2$ or I_2. The substitutions probably go through an addition-elimination pathway, involving the intermediate sulphur-stabilised cation (**8**). Elimination would be favoured, rather than addition, because of extreme steric crowding in addition products.

The anion of (**1**, $R^1 =$ Me) also opened ethylene oxide in *ca.* 80% crude yield to give the allenol (**9**, $R^1 =$ Me). This cyclised rapidly, even on silica gel, to give the dihydropyran (**10**), although (**9**, $R^1 =$ H) is reported[9] to cyclise to the dihydro-oxole (**11**).

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