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ADDITION OF LITHIUM DIMETHYLCUPRATE TO AN ALLENIC KETONE EVIDENCE FOR A CARBON-CARBON DOUBLE BOND 1-2 ADDITION

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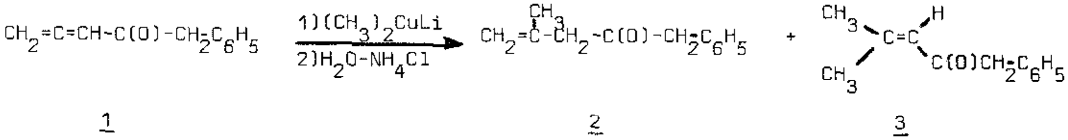
There have been many synthetic applications of the addition of lithium dialkylcuprates to α-β unsaturated ketones (1). However little is known about the actual mechanism of this reaction (2). This is most commonly reported as a 1-4 addition process leading to an intermediate lithium enolate but other transient species could be taken into account (3).

In the preceding communication (8) we have established that the addition of lithium dimethylcuprate to an allenic phosphine oxide should proceed via a 1-2 addition to the activated carbon-carbon double bond. We wish to report now that a similar reaction process applies in the case of the allenic ketone 1 (4) .

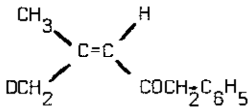
The addition of lithium dimethylcuprate to 1, followed by protonation results in a mixture of two isomeric adducts 2 and 3. The compound 2 is the major product and the ratio 2/3 depends on the experimental conditions: time, temperature, presence of a complexing agent (runs 10-18) but not on the hydrolysis temperature itself (runs 17-18, Table II).

Scheme 1

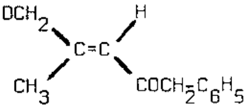


From these results equilibria between various organometallic species (some of them leading to 2 and others to 3) were likely to occur.

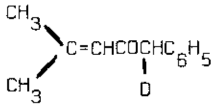
Treatment of 2 by an equivalent amount of sodium hydride in ether gives, after protonation, 3 excusively (whatever the hydrolysis temperature be). This leads us to postulate that, in scheme 1, 3 arises from the hydrolysis of an enolate species. In order to determine the nature of the metal associated to this enolate we compared the deuteration of the intermediates resulting from the addition of lithium dimethylcuprate to 1 and that of the anionic species resulting from treatment of 2 and 3 by sodium hydride (Table I).



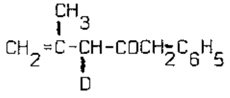
3a



3b



3c



$CH_2{=}\overset{CH_3}{C}{-}\underset{D}{C}H{-}COCH_2C_6H_5$

2a

Table I

Run	Ketones	Experimental conditions	2a	3a	3b	3c	Overall yield (%)
			(%)				
1	1	1) $(CH_3)_2CuLi$, -23°, 15mn 2) D_2O-NaCN	80	20	0	0	80
2	2 + 3	1) NaH, 36°, 30mn 2) D_2O, -23°	0	30	30	40	90
3	3	1) NaH, 36°, 30mn 2) D_2O, -23°	0	0	0	100	80

It must be pointed out that in run 1 3b and 3c could not be detected. Thus the formation of lithium enolate in the reaction mixture resulting from the addition of lithium dimethylcuprate to 1 seems to be unlikely (5). This is comfirmed by the fact that the addition of one equivalent of methyl-copper tributylphosphine complex does not affect the ratio 2/3 within experimental error (run 20).An inverse phenomenum has been observed with the allenic phosphine oxide where the lithium species was present (8). Thus in scheme 1 3 should arise from hydrolysis of a copper enolate species.

All the results could be rationalised by an equilibrium between two different copper species 4 and 5 (Scheme 2).

Scheme 2

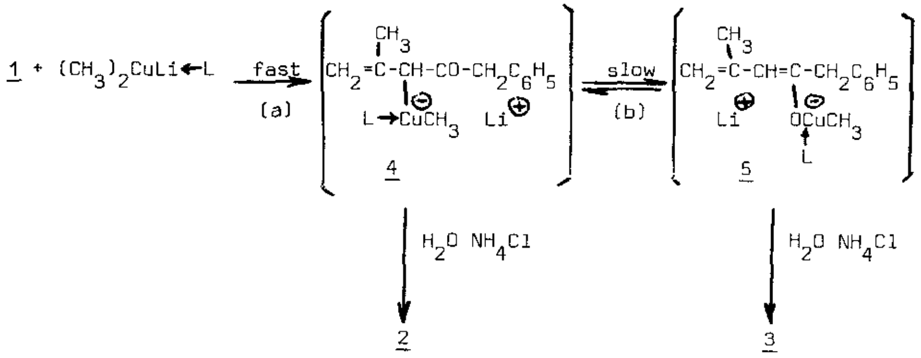


TABLE II

REACTION OF LITHIUM DIMETHYLCUPRATE AND LITHIUM DIMETHYLCUPRATE-TRI(N-BUTYL) PHOSPHINE WITH THE ALLENIC KETONE 1.

Run (a)	Temp. (°C)	Reaction time (hours)	$(CH_3)_2CuLi$ (b)		$(CH_3)_2CuLiP(nC_4H_9)$ (b)	
			2 (%)	3	2 (%)	3
10	- 23	0.15	82	18		
11	- 23	0.5	60	40	74	26
12	- 23	1.5	60	40	74	26
13	- 77	0.15	95	5		
14	- 77	0.5	81	19	86	14
15	- 77	1.5	75	25		
16	- 77	3	75	25	86	14
17	- 23	1.5				
	then - 77	1.5	77	23	85	15
18	- 23	1.5				
	then - 77	(c)	60	40		
19	- 77	1.5				
	then - 23	0.5	62	38		
20	- 23	0.5				
	(d)	1	62	38		
21	- 23	0.5	47	53		
22	- 23 (f)	0.5	32	68		

(a) The ketone 1 (1 mmole in 5 ml. ether) was added to the cuprate (1 mole in 5ml of ether) under argon atmosphere. Overall yields of isolated products are 80-90 %.

(b) 2/3 ratio (± 2 %), average value from at least two identical runs, was determined on the crude product form NMR spectra and GC. This ratio remains unchanged after purification by preparative TLC.

(c) immediately hydrolysed at - 77°C.

(d) one equivalent of $CH_3Cu-P(nC_4H_9)_3$, ILi was added at - 23°C and the hydrolysis was made 1 hour later.

(e) four equivalents of NNN'N' tetramethylethylenediamine were added.

(f) one equivalent of cuprous iodide was added to an ether solution of alcoholate of (-) N-methylephedrine at 0°C, followed by an equivalent of methyllithium. Allenic ketone was then added at - 23°C.

The displacement of the equilibrium (b) towards the copper enolate 5 can be achieved by addition of hard ligands (runs 21,22). An inverse displacement is observed with tributylphosphine (9).

In conclusion a 1-4 addition can hardly explain all these phenomena. It appears that the reaction of lithium dimethylcuprate with the allenic ketone 1 should proceed via a 1-2 addition to the carbon-carbon double bond.

A similar conclusion was drawn by Posner and Lentz from the addition of lithium dimethylcuprate to substituted cyclopentenones (7).

Attempts to confirm our mechanistical hypothesis by a spectroscopic study of the intermediates are in progress.

REFERENCES AND NOTES

(1) For a comprehensive review see G. H. POSNER Org. Reactions, 19, 1, (1972)

(2) a) J. MUNCH-PETERSEN and V. K. ANDERSON Acta Chem. Scand. 15, 271, (1961)

b) H. O. HOUSE, W. L. RESPESS and G. M. WHITESIDES J. Org. Chem., 31, 3128 (1966); for a recent discussion see H. O. HOUSE Acc. Chem. Res., 9, 59 (1976)

c) H. RIVIERE and Ping WAH-TANGC. C. Acad. Sci.,C,274, 1944 (1972)

(3) Some evidence for copper enolate transient species has been reported in the case of the addition of magnesium diphenylcuprate to an α-β unsaturated ketone ; see (2c).

(4) Only one example of lithium dialkylcuprate addition to an allenic ketone has recently been reported. J.C. DAMIANO, J.L. LUCHE, J.P. CRABBE Tetrahedron Letters, 779 (1976)

(5) The replacement of lithium by sodium should not drastically influence the nature and the proportions of deuterated products.

(6) Attempts to reestablish organo-copper intermediates via the following sequence failed:

$$\underline{2} + \underline{3} \xrightarrow[36°]{\text{NaH,LiI}} \xrightarrow[-23°]{CH_3Cu,P(n\text{-}Bu)_3,LiI} \xrightarrow{H_2O\ NH_4Cl} \underline{3}$$

This confirms the absence of an equilibrium between copper complex 4 and lithium enolate

(7) G. H. POSNER and C.M. LENTZ private communication

We thank Pr. Gary H. POSNER for discussions along these lines prior to publication.

(8) J. BERLAN, J-P. BATTIONI and K. KOOSHA, preceding communication

(9) This effect can be explained by the symbiotic rule. C.K. JORGENSEN Inorg. Chem., 3, 1201 (1964)