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1-4 ADDITION OF CARBANIONS TO α-β UNSATURATED CARBONYL COMPOUNDS IN THE PRESENCE OF HMPA : FIRST EVIDENCE OF KINETIC CONTROL.

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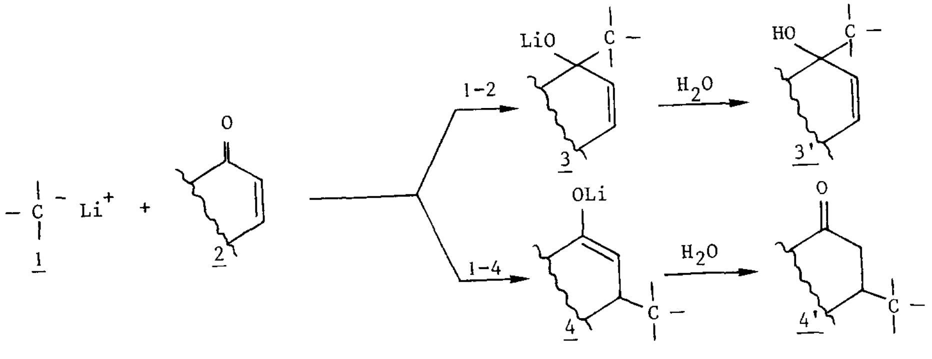
Summary : 1-4 addition of some carbanionic species is enhanced if HMPA is added to the carbanion prior α-enones. Examples of 1-4 additions occuring under kinetic control are disclosed.

It has been recently described[1-4] that 1-4 addition of lithiated carbanions 1 to α enones 2 is highly favoured in presence of HMPA, a strong solvating agent of lithium cation (Scheme I).

SCHEME I

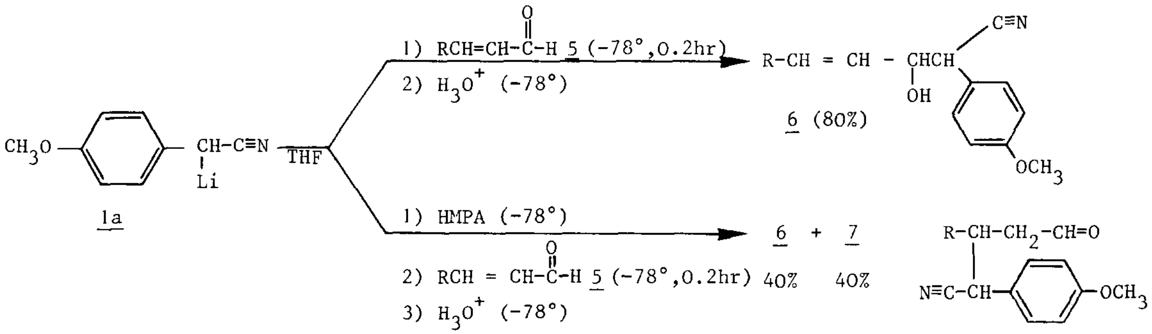


This result agrees with theoretical calculations according to which 1-4 addition is expected when the lithium cation is unable to complexe the carbonyl group of the α enone[5].
However in nearly all the cases studied[6] it was impossible to assess if the 1-4 addition, leading to 4, observed when HMPA is present prior the addition of enone to the carbanion, is a kinetically or a thermodynamically controlled process. In these cases the formation of the 1-2 adduct 3, observed in THF, was found to be highly reversible when HMPA is added to the medium at the same temperature[1-3, 7].

We have recently observed, independently and simultaneously in our two laboratories, reactions of lithiated carbanions 1a and 1b with α,β-unsaturated carbonyl compounds for which addition of HMPA to a THF solution of the carbanion not only increases - as previously observed - the amount of 1-4 addition, but also secures it under kinetic control.

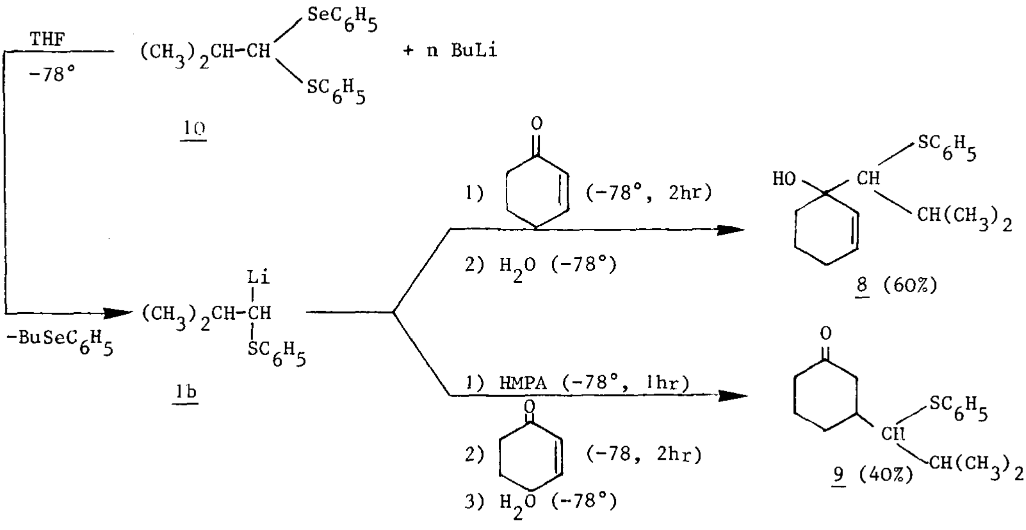
Thus when lithiated p-methoxy-phenyl acetonitrile 1a reacts with crotonaldehyde 5 (R : CH_3) or cinnamaldehyde 5 (R : C_6H_5) in THF at -78°, only 1-2 addition takes place[15a] leading to diastereoisomeric allyl alcohols 6 in 80% yield. In THF-HMPA (80 : 20) however both the 1-2 6 and the 1-4 7 adducts are obtained in equal amount (-78°, 80% overall)[15b].

SCHEME II



Similarly it was found that whereas 1-lithio-1-thiophenyl-2-methyl propane 1b (prepared from n BuLi and 1-thiophenyl-1-selenophenyl-2-methyl propane 10 at -78° in THF)[12] adds exclusively 1-2 to cyclohexenone (60% yield in 8)[16a], the 1-4 adduct 9 (40% yield) was the only one observed when the reaction is performed in a THF-HMPA (80 : 20) mixture[16b] (Scheme III).

SCHEME III



Identical 1-4 addition was already disclosed by Dolak and Bryson[13] using the same carbanion 1b prepared by metalation of 1-thiophenyl 2-methyl propane (tBuLi/THF.HMPA - the HMPA is absolutely needed for the success of the metalation).

In both cases, disclosed on scheme II and III, the 1-4 addition was found to occur under kinetic control. The lithium alcoholates corresponding to the 1-2 adducts 6 and 8 do not lead to the 1-4 adducts 7 and 9 when HMPA is added to the reaction mixture after consumption of the enones (at -78°C, respectively for 1 or 2hr).
Purified 8 was also transformed to the corresponding lithium alcoholate (nBuLi, THF/HMPT 80:20, -78°) and maintained at -78°C for two hours prior hydrolysis. In all these experiments allylic alcohols 6 and 8 were quantitatively recovered without any trace of 1-4 addition products 7 or 9 (IR, NMR, TLC).

Thus, addition of HMPA to the carbanion solution, prior addition of α enones, is at least in the two cases just described a sine qua non condition for favoring the 1-4 addition which occurs under kinetic control.

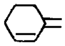
This observation is very important since it should allow a simple method for 1-4 adduct synthesis in cases where no other methods are available.

Finally it must be pointed out that the kinetically controlled 1-4 addition strictly depends on the conditions used, and on the nature of the two reagents :
Whereas 1-4 addition can be observed only under kinetic control between lithiated p methoxy phenyl acetonitrile 1a and crotonaldehyde 5 (THF : HMPT 80 : 20, -78°, 0.2h scheme II), 1-4 addition can be performed under thermodynamically controlled conditions when the closely related lithiated m chloro phenyl acetonitrile[14] is substituted to 1a. And 1-lithio-1-thiophenyl-2-methyl propane which needs HMPA to add 1-4 to cyclohexenone (at -78°C) exclusively reacts 1-4 with chalcone in THF at the same temperature (80% yield).

Work is in progress in both laboratories to apply the new observation in organic synthesis especially for HMPA mediated acyl anions 1-4 addition. Preliminary results agree with the finding disclosed in this report.

References and Notes

1. R. Sauvêtre and J. Seyden-Penne, Tetrahedron Lett. 3949 (1976) ; R. Sauvêtre, M.C. Roux-Schmitt and J. Seyden-Penne, Tetrahedron 34, 2135 (1978)
2. W.C. Still and A. Mitra, Tetrahedron Lett. 2659 (1978) These authors have shown that 1-4 addition is under kinetic control in THF-HMPA with Me_3SiLi. However, they did not perform similar experiments with Me_3CLi.
3. J. Luchetti and A. Krief, Tetrahedron Lett. 2697 (1978)
4. B. Deschamps, Tetrahedron 34, 2009 (1978)
5. A. Loupy and J.M. Lefour, Tetrahedron 34, 2597 (1978)

6. Kinetic control of 1-4 addition in THF-HMPA has been observed from lithiated phosphonate (EtO)$_2$P(O)$\bar{C}$HCN/Li$^+$ and 2-cyclohexenone[4] due to the fact that 1-2 addition is followed by a rapid step, leading to the diene  CH-C≡N, so that it is not reversible.
7. 1-2 addition was also found to be reversible in THF[8-11] by performing the reactions for sufficently long time or by raising the temperature.
8. A.G. Schultz and Y.K. Yee, J. Org. Chem. 41, 4044 (1976)
9. P.C. Ostrowski and V.V. Kane, Tetrahedron Lett. 3549 (1977)
10. E.M. Kaiser, P.L. Knutson and J.R. McClure, Tetrahedron Lett. 1747 (1978)
11. S. Yama-Giwa, N. Hoshi, H. Sato, H. Kosugi and H. Uda, J.C.S. Perkin I, 214 (1978)
12. a) D. Seebach and A.K. Beck, Angew. Chem. int. ed. 13, 806 (1974)
    b) A. Anciaux, A. Eman, W. Dumont and A. Krief, Tet. Lett. 1617 (1975)
    c) D. Seebach, N. Meyer and A.K. Beck, Liebigs Ann. Chem. 846 (1977)
    d) This carbanion was also prepared from the corresponding α-bromosulfide and nBuLi in THF. W. Dumont and A. Krief, results to be published.
13. T.M. Dolak and T.A. Bryson, Tetrahedron Lett. 1961 (1977)
14. L. Wartski, M. El Bouz and J. Seyden-Penne, J. Organomet. Chem. to be published
15. Experimental.
    a) To a solution of 1a ($5\ 10^{-3}$mol) in THF (22ml) is added n-BuLi ($5\ 10^{-3}$ mol, 1.6 M. in hexane). After 0.2hr at -78°, 5 (5.10^{-3}mol) in THF (5ml) is added. Stirring is continued for another 0.2hr before addition of HCl (10% aqueous). After usual work up the residue is analyzed by TLC, IR, NMR. Only 6 and a small amount of 1a are detected.
    b) To a solution of 1a ($5\ 10^{-3}$ mol) in THF-HMPA [(80-20), 20 ml] is added at -78°, nBuLi ($5\ 10^{-3}$ mol). After 10 mn stirring at -78°C, 5, 5.10^{-3} mole in THF (5ml) is added. The reaction mixture is worked as previously after 10 mn at -78°C. A mixture of 6 and 7 is obtained : they are characterized by TLC, IR, NMR.
16. Experimental.
    a) To a solution of (4.10^{-3} mole, 1.29g) 1-phenylthio-1-phenylseleno-3-methyl-propane in THF (10 ml), is added, at -78°C, $4.1\ 10^{-3}$mole of nBuLi (2.05 N in hexane). The mixture is stirred for 0.5 hr at -78°C. Cyclohexenone (4.10^{-3} mole, 0.384 g) in THF (2ml) is then added. After 2hr at -78°C, the mixture is hydrolysed at low temperature.
    After usual work up, the residue is analyzed by TLC and NMR : only the 1-2 adduct is detected. Purification of the crude mixture (PLC on Silicagel, ether/pentane 20/80) affords the 1-2 adduct in 60% yield (0.62 g).
    b) 1-phenylthio-1-phenylseleno-2-methylpropane (1.10^{-3} mole, 0.32g) in THF (3ml) is reacted for 0.5 hr at -78°C, with 1.10^{-3}m of n BuLi (2.05 N in hexane). HMPT ($2.5\ 10^{-3}$m, 0.448 g) is then slowly added and the mixture is stirred for 1hr at -78°C. Cyclohexenone ($1.05\ 10^{-3}$m, 0.1 g) in THF (1 ml) is then introduced and the resulting mixture is stirred for 2hr at -78°C Hydrolysis at low temperature followed by usual work up gives a residue in which only the 1-4 adduct can be detected by TLC.
    PLC on silicagel (ether/pentane 20/80) affords the 1-4 adduct in 40% yield (0.104 g).

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