Tetrahedron Letters,Vol.25,No.32,pp 3463-3466,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

ULTRASOUND IN ORGANIC SYNTHESIS 6[1].
AN EASY PREPARATION OF ORGANOZINC REAGENTS AND THEIR CONJUGATE ADDITION TO α-ENONES

Christian Petrier, Jean-Louis Luche*, Claude Dupuy
Université Scientifique et Médicale de Grenoble
Laboratoire d'Etudes Dynamiques et Structurales de la Sélectivité
Bat. 52 - Chimie Recherche
B.P. 68
38402 - SAINT MARTIN D'HERES CEDEX - FRANCE

Summary : Sonication allows the efficient preparation of various organozinc reagents, which cleanly add in a conjugate fashion to α-enones in the presence of Ni(acac)$_2$.

We recently reported the preparation of diarylzinc reagents by ultrasonic irradiation of a mixture of aryl bromides, zinc bromide and lithium in ethereal solvents (diethyl ether, tetrahydrofuran) and their conjugate addition to α-enones[2].

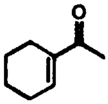
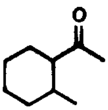
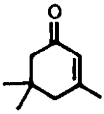
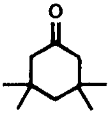
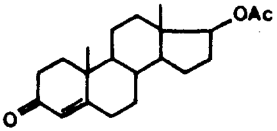
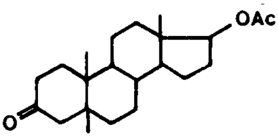
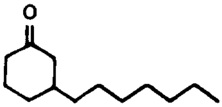
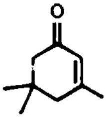
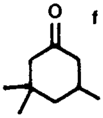
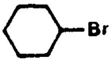
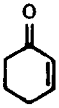
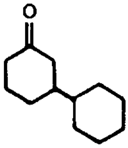
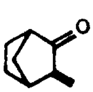
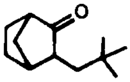
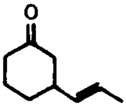
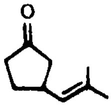
Preliminary experiments revealed that, except for methyl iodide[3], the method was not successful for the preparation of the dialkyl analogs. This limitation has now been overcome and we wish to report a modification which allows a generalization of the procedure.

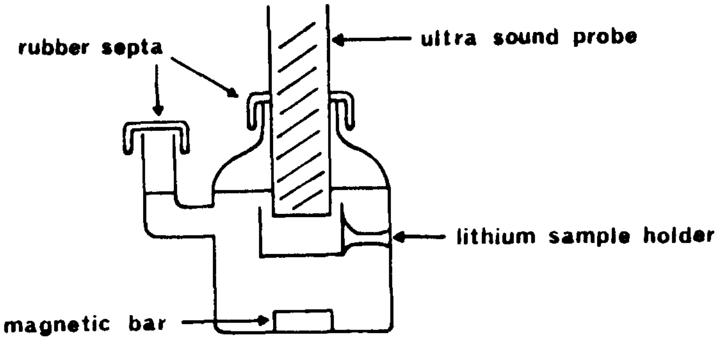
A mixture of an organic halide, lithium and zinc bromide are sonicated with a cell-disruptor type generator[4] in a glass reactor as shown in the figure. The usual solvent is a mixture of toluene and THF (ca. 85-15) which allows a very rapid transformation to the desired organometallic species[5]. The reaction is generally completed in 10-20 min. at 0°C (ice water cooling bath) and the reagent is formed in essentially quantitative yield. When compared to previous experiments run in a common ultrasonic cleaner, the reaction occurs much more rapidly, with an excellent reproducibility. The improvement appears to be essentially due to a better control of the sonication conditions (temperature, energy).

The ability of the reagents thus obtained to add conjugatively to α-enones was tested on various substrates. Addition was found to occur efficiently at room temperature in the presence of 1 % of the stoichiometric amount of Ni(acac)$_2$. After work-up and purification of the reaction mixture, the expected ketone is isolated in high yield. Representative exam-

Table

$$\mathrm{R-X} + \mathrm{Li} + \mathrm{ZnBr_2} \xrightarrow{\text{Ultrasound}} \mathrm{R_2Zn, nLiX} \xrightarrow[\mathrm{Ni(acac)_2}]{\text{enone}} \text{Adduct}$$

Halide	Enone	Adduct[a]	Yield %	
			1-4 add.	Litt. Yield
CH_3I		 [b]	73	93[c]
CH_3I			90	88[d]
CH_3I			67	20[e]
n - $C_7H_{15}Br$			88	
n - $C_7H_{15}Br$		 [f]	69	
			40	
t - C_4H_9Br			78	
			83	-[g]
			21	



NOTES FOR THE TABLE

[a] Typical procedure : 10 mmol halide, 5 mmol (1,115 g) $ZnBr_2$, 140 mg Li wire in 20 mL toluene and 3 mL THF are sonicated at 0° for 10-20 min. 5 mmol of the enone and 20 mg $Ni(acac)_2$ in 1 mL THF are then added to the black mixture and the reaction is monitored by TLC. After completion (5 Min.-2 hr), the mixture is quenched (aq. NH_4Cl) and worked-up as usual. Purification is made by column chromatography (SiO_2). Yields are given for the isolated purified material. All new compounds gave satisfactory analytical data.[b] Mixture of epimers.[c] Yamamoto, Y. ; Yamamoto, S. ; Yatagai, H. ; Ishikara, Y. ; Maruyama, K. J. Org. Chem. 1982 47 119. [d] See ref. 6.[e] Birch, A.J. ; Smith, M. Proc. Chem. Soc. 1962 356. [f] This reaction is also observed with pulegone and carvone. [g] Yield not given. Casey, C.P. ; Boggs, R.A. Tetrahedron Lett. 1971 2455.

---

ples are given in the table.

From these results, the general comments can be made :

a - as shown previously[3], methylation occurs very easily and the method appears to be of broad applicability.

b - introduction of primary, secondary and even tertiary groups occurs in synthetically useful yields.

d - virtually no 1-2 addition is observed. In the absence of $Ni(acac)_2$, the reaction occurs more slowly. The formation of the allylic alcohol was never detected. In contrast in the absence of transition metal catalysts trimethyl aluminium is known to add to the carbonyl of α-enones[6].

e - a limitation of the method is met for the addition of reducing reagents, i.e. those possessing hydrogen atoms β to the metal, to hindered substrates. In this case reduction occurs preferentially and the yields in saturated ketones are high.

Contrasting with many organocopper reagents[7], organozinc derivatives are thermally stable and their preparation under sonochemical conditions can be performed under extremely simple conditions. Thus, an alternative to the popular organocopper reagents[8] is offered and the method reported here should find many applications in organic syntheses. A detailed study of scope of this selective method, as well as the mechanistic aspects of the sonication and addition steps are under further investigation, and will be reported in a next paper.

Acknowledgements : The authors thank the CNRS (ATP Chimie Fine, LA 332) for financial support. Thanks are due to Prof. A. Rassat and Dr. A.E. Greene for their interest in this work, and to Prof. E. Negishi for a stimulating discussion.

References

1. Previous paper in this series : Luche, J.L. ; Petrier, C. ; Dupuy, C. Tetrahedron Lett. 1984 25 753.
2. Luche, J.L. ; Petrier, C. ; Lansard, J.P. ; Greene, A.E. J. Org. Chem. 1983 48 3837.
3. Greene, A.E. ; Lansard, J.P. ; Luche, J.L. ; Petrier, C. J. Org. Chem. 1984 49 931.
4. Ultrasons Annemasse generator, operating at 30 KHz, with adjustable energy output.
5. Solvents in sonochemical reactions have to meet some specific requirements (volatility, viscosity, surface tension) for optimum yields. These important and complex effects will be discussed later. For examples see : Suslick, K.S. ; Gawienowski, J.J. ; Schubert, P.R.; Wang, H.H. Ultrasonics 1984 22 33. Sehgal, C. ; Yu, T.J.; Sutherland, R.G. ; Verrall, R.E. J. Phys. Chem. 1982 86 2982.
6. Bagnell, L. ; Jeffery, E.A. ; Meisters, A. ; Mole, T. Austr. J. Chem. 1975 28 801.
7. For thermally stable copper derivatives see : Bertz, S.H. ; Dabbagh, G. J. Chem. Soc. Chem. Commun. 1982 1030.
8. Posner, G.H. An introduction to syntheses using organocopper reagents Wiley.Interscience New York, N.Y 1980.

(Received in France 22 April 1984)