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ULTRASOUND IN ORGANIC SYNTHESIS 9 [1]
FURTHER RESULTS FOR THE BOUVEAULT REACTION

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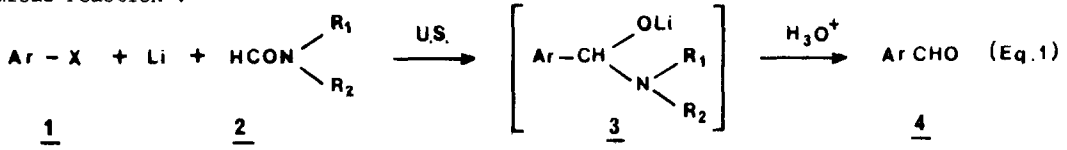
Summary : The Bouveault reaction under ultrasonic irradiation can readily be effected from various amides and the effect of the solvent was studied. In the case of diethylether, results are strongly dependent on the wave frequency.

Aromatic lithium reagents permit, through the Bouveault reaction, the one-carbon homologation to the corresponding aldehyde. This process depicted in Eq.(1) proceeds via the α-aminoalkoxide intermediate 3, and was shown to be efficiently achieved from the halide in a one step sonochemical reaction[2].



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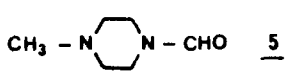

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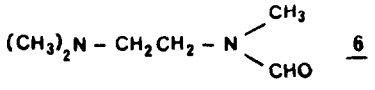

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In this note some new results are reported which should find their value in future synthetic developments[3], and in the knowledge of the interaction of sonic waves with reactive systems. The model chosen for the tests was the reaction of bromobenzene with lithium and several amides. In our first report[2], this reaction was effected with dimethylformamide (DMF) in tetrahydrofuran (THF). Some recent papers[4] mention the use of more or less elaborated (and expensive) formamides for better yields. Comparative experiments were then conducted with DMF, N-formyl-N'-Methyl-piperazine 5 and N,N,N'-trimethyl-N'-formyl-ethylenediamine 6[5]. In parallel, the solvent was changed from THF to tetrahydropyran (THP) and diethylether. The conclusions of this study, summarized in the table are the following :

Similar results, i.e. yields of benzaldehyde, are obtained from the 3 amides tested. This observation means that the stabilizing factor in intermediate 3 by a supplementary coordinating atom, present in 5 and 6, absent in DMF, is of minor importance.

Whereas the difference between THF and THP as solvents is small, using diethyl ether provided an important observation.

Table

Amide	Solvent	Sonication[a]	Yield[b]
DMF	THF	10 min. 50 KHz	81
	THP	10 min. 50 KHz	76
	Et_2O	30 min. 50 KHz	75
5	THF	10 min. 50 KHz	80
	THP	10 min. 50 KHz	75
	Et_2O	45 min. 500 KHz	77
6	THF	10 min. 50 KHz	64
	THP	10 min. 50 KHz	74
	Et_2O	30 min. 500 KHz	76

[a] Sonications were run at 15-18°C, using 2mmol ϕ Br, 2mmol amide and 4mmol lithium (with 2% Na, from Alfa). Using a 1% Na alloy lead to extremely slow reactions (50% in 8hrs).

[b] VPC yields with internal standard (tetradecane).

In a common ultrasonic cleaning bath (50 KHz), the reactions effected in this solvent occurred in significantly longer times (with DMF) or not at all (with 5 and 6). However, using a 500 KHz wave permits to recover the efficiency of the ultrasonic process. This result has to be underlined as the number of examples of frequency dependent reactions is exceedingly small[6]. Experiments run with other alkali metals, sodium and potassium which are excellent promoters for a similar reaction with isocyanates[7], gave mixtures of benzaldehyde (low yields) and benzyl alcohol.

In conclusion, the sonochemical Bouveault reaction, when applied to aromatic substrates, can be effected with similar efficiencies from various amides. The choice of a particular system can therefore be made by considering the following synthetic steps, examples of which are given in the accompanying paper.

Literature

1. Previous paper in this series, see : Einhorn,C. ; Luche,J.L. Carbohydr. Res. submitted.
2. Petrier,C. ; Gemal,A.L. Tetrahedron Lett. 1982 23 3361.
3. See accompanying paper.
4. For instance, see Comins D. ; Meyers,A.I. Synthesis. 1978 403.
5. Preparation of 5 and 6 was simply achieved by mixing the amines (Aldrich) with formic acid (1 equiv) in toluene, followed by azeotrope distillation and final distillation of the pure compounds.
6. For a significant example see : Saracco,G. ; Arzano,A. Chim. Ind. (Milano). 1968 50 314.
7. Einhorn,J. ; Luche,J.L. Tetrahedron Lett. 1986 27 0000.

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