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SELECTIVE TIN AND ZINC MEDIATED ALLYLATIONS OF CARBONYL COMPOUNDS IN AQUEOUS MEDIA[1]

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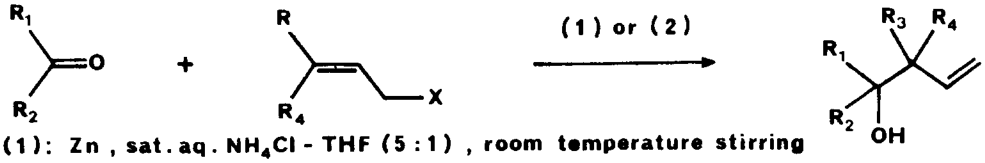
Summary : Aldehydes undergo preferential allylation in the presence of ketones by the tin or zinc mediated method, easily effected in aqueous media.

Allylations of carbonyl compounds to homoallylic alcohols is an important synthetic pathway[2]. Its high potential in the build-up of some natural compounds has stimulated numerous studies and methods utilizing organometallics derived from aluminum , boron, chromium, tin, titanium[2] and cerium[3] have been developed.

We recently reported the unexpected reaction of allylic halides with aldehydes and ketones in the presence of zinc in aqueous media[1]. Homoallylic alcohols are obtained in yields of synthetic value by this mechanistically intriguing process. Since then, we have found that this reaction can also be efficiently performed by using metallic tin under sonication in a water-tetrahydrofuran mixture to afford the rearranged homoallylic alcohol[4].



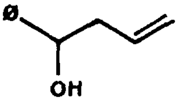
(1): Zn , sat.aq. NH_4Cl - THF (5 : 1) , room temperature stirring

(2): Sn , H_2O - THF (5 : 1), sonication

Although these reactions occur in good yields from aldehydes and ketones as well, we investigated the possibility of a kinetic selectivity permitting a discrimination between these two functionnalities.

Intermolecular competitive experiments revealed that such a selectivity is easily obtained, as demonstrated in the following examples :

1- An equimolar mixture of benzaldehyde and acetophenone was reacted with allyl bromide and zinc[6] (1.2 equiv each) in saturated aqueous NH_4Cl : THF (5 : 1,v : v) at room temperature for 30 min. VPC analysis[7] revealed that 1-phenyl-3-butene-1-ol 1 was formed in 86% yield whereas acetophenone was recovered pratically unaffected (4% reaction only).



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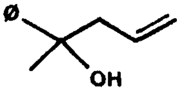

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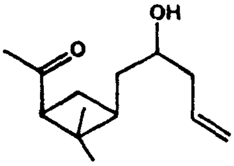

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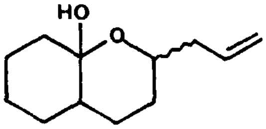

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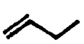
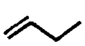
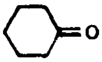
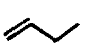
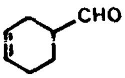
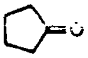
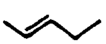
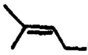
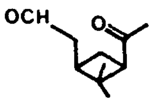
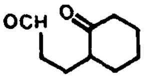
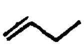
Table

Aldehyde	Ketone	Halide (equiv)	Metal (equiv)	% Addition[a] to aldehyde	to ketone
Ø CHO	Ø COCH$_3$	 Br (1.2)	Zn (1.2)	86	4
		 Br (1.2)	Sn (1.2)	90	0
Ø CHO		 Br (1.5)	Zn (1.5)	87	0
		 Br (1.2)	Sn (1.2)	98	11
		 Br (1.2)	Zn (1.2)	87	0
		 Br (1.2)	Sn (1.2)	100	0
		 Br (1.2)	Zn (1.2)	94[b]	0
		 Br (1.2)	Sn (1.2)	99[b]	trace
		 Cl (1.2)	Zn (1.2)	100[b]	0
		 Br (1.5)	Zn (1.5)	94 (92)[c]	0
		 Br (1.2)	Sn (1.2)	100 (98)[c]	0
		 Br (1.2)	Zn (1.2)	(55)[d,e]	0
		 Br (1.2)	Sn (1.2)	(70)[e]	0

[a] Addition products were identified by comparison with authentic samples. Yields were calculated from VPC diagrams. Figures in parenthèses refer to isolated yields of purified material. [b] Mixture of stereoisomers with allylic transposition. [c] A single stereoisomer was obtained (unknown configuration). [d] Materiel balance consists only in a gummy polymer. [e] Isolated as a ca 1:1 mixture of stereoisomeric hemiketals 4, which can be resolved by column chromatography.

2- An equimolar mixture of benzaldehyde and acetophenone was sonicated[8] in the presence of allylbromide and tin (1.2 equiv. each) in distilled water : THF (5 : 1) at room temperature for 30 min. Again, a highly selective reaction was observed as 90% of the aldehyde was converted to the desired alcohol with no trace of reaction on the ketone.

In both cases, no reduction products such as benzyl alcohol, 1-phenyl ethanol, or the pinacols corresponding to the initial carbonyl compounds were detected in the reaction mixture.

That the observed selectivity towards the aldehyde function is probably due to a kinetic control is supported by the following observation . acetophenone was reacted with allyl bromide and zinc as described above. After completion of the reaction 1 equiv of benzaldehyde was added. Under such conditions, the aldehyde component of the mixture was left unchanged, and compound 2 was formed in 50% yield.

Generalization of the process was attempted and several aldehyde ketone pairs were submitted to the procedures. Results are given in the table[9].

Of greater importance are the intramolecular competition experiments. We have shown that a high degree of selectivity is also obtained, in agreement to the results obtained from mixtures. As typical examples, the reactions with pinonaldehyde were performed as follows :

pinonaldehyde[10] (840 mg, 5 mmol), allyl bromide (900 mg, 7,5 mmol) and zinc powder (490 mg, 7,5 mmol) were stirred in 5 mL of aq. sat. NH_4Cl and 1 mL of THF for 30 min. Extraction with ether and usual work-up of the organic phase gave an oil which was chromatographed (SiO_2). Compound 3 was obtained as an oil in 92% yield[11].

Pinonaldehyde (1,68g, 10 mmol), allyl bromide (1,36g, 12 mmol) and tin powder (1,4g, 12mmol) were sonicated for 30 min at room temperature in 5 mL of distilled water and 1 mL of THF. The white tan viscous mixture was treated with aq. HCl and sat. aq. NH_4Cl, extracted with ether and worked-up as usual to give 2,52g of an oil. Purification on a silica gel column gave 2,08g of pure 3 (98%).

Such highly preferential reaction have not frequently been described. Seebach et al have discussed this point and shown that titanium derivatives are able to react selectively with aldehydes in the presence of ketones[12]. Our results show that equivalent selectivities can be reached with great ease using unexpensive common metals in aqueous media. Although the present results are limited to the addition of allylic group, applications in synthesis are under further development.

Acknowledgements : The authors thank Dr. A.E. Greene for fruitful discussions, and CNRS (ATP Chimie Fine) for financial support.

Literature

1. C. Petrier, J.L. Luche J. Org. Chem. 1985 in press.

2. For recent reviews, see Hoffmann, R.W. Angew Chem Int Ed Engl 1982 21 555-566. Yamamoto, Y. ; Maruyama , K. Heterocycles 1982 18 357-386.

3. Imamoto, T. ; Kusumoto, T. ; Tawarayama, Y. ; Sugiura, Y. ; Mita, T. ; Hatanaka, Y. ; Yokoyama, M. J. Org. Chem. 1984 49 3904-3912.

4. Several recent papers report the allylation of C=O groups, using a mixture of aluminum and tin in a two phase system consisting in diethylether and aqueous hydrogen bromide[5]. The method that we presently develop makes use of tin powder under neutral conditions with an improved efficiency. Its selectivity and generality will be discussed in a future paper.

5. Nokami, J. ; Wakabayashi, S. ; Okawana, R. Chem Letters 1984 869-870 and ref. cited. See also : Uneyama, K. ; Matsudo, H. ; Torii, S. Tetrahedron Lett 1984 25 6017-6020.

6. Zinc powder (Merck, <60 μm) was used as received.

7. Erba Science Fractovap 2100 chromatograph, equipped with a Carbowax 20 M (2m x 2mm) column. Peaks were identified by coinjection with authentic samples.

8. Ultrason Annemasse 30 KHz probe sonicator. Satisfactory results are also obtained with a Sonoclean 50 KHz ultrasound cleaning bath. Tin (powder from Fluka) was used as received.

9. All new compounds gave satisfactory spectral and analytical data.

10. Prepared by ozonolysis of α-pinene according to : Eshinazi, H.E. J. Org Chem 1961 26 3072-3076.

11. Compound 3 : IR(neat) : 3450, 3060, 1700, 1640, 910 cm^{-1}. NMR(CDCl$_3$) : 6.3-5.5(m,1H), 5.3-4.9(m,2H), 3.6(quint, 1H), 2.9(t,1H), 2.4-1.0 (m,8H), 2.05(s,3H), 1.3(s,3H), 0.9 (s,3H)ppm M.S.m/e 211(M+1)$^+$, 193, 119, 99, 71.
Compounds 4 were obtained by the same procedures : 4a (less polar isomer) m.p. 44-44.5 (pentane, -40°C).I.R.(KBr) : 3350, 3060, 2900, 2830, 1640, 1440 cm^{-1}. NMR(CDCl$_3$, 80MHz Brucker spectrometer) : 6.2-5.5(m,1H), 5.3-4.8(m,2H), 4.2-3.5(m,1H), 2.5-1.0(m,16H).M.S. m/e : 196(M$^+$), 179,98,87,81,72,69,59. 4b(more polar isomer) m.p. 46.5-47.5(pentane, -40°C). I.R.(KBr) : 3300, 3060, 2900, 2850, 1635, 1440 cm^{-1}. NMR : practically identical to the spectrum of 4a. M.S m/e : 196, 178, 155, 137, 111, 98, 81, 68.

12. Weidmann, B. ; Seebach, D. Angew Chem Int. Ed Engl 1983 22 31-45. For a recent example of selective alkylation using organotitanium compounds see : Kostova, K. ; Hesse, M. Helv. Chim. Acta 1984 67 1713-1724.

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