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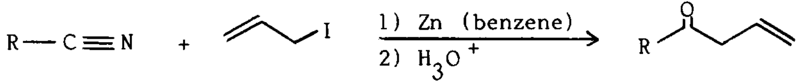
IMPROVED SYNTHESIS OF β,γ-UNSATURATED KETONES BY THE REACTION OF ALLYLIC ZINC BROMIDES WITH NITRILES.

By G. Rousseau and J.M. Conia

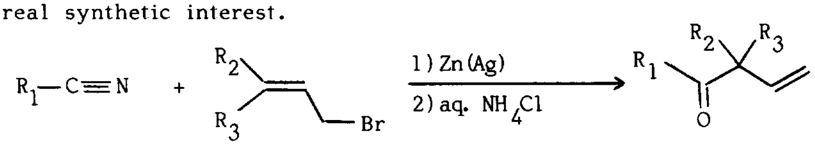
Laboratoire des Carbocycles*, Université de Paris-Sud, Bâtiment 420
91405 ORSAY, France

Summary. The reaction of allylic bromides with nitriles in the presence of Zn-Ag couple leads, after hydrolysis, to β,γ-unsaturated ketones in high yield.

In 1901, Blaise reported the reaction of allyl iodide with nitriles in the presence of zinc leading to allyl ketones (1). But the yields of the method and in the mean time the discovery of Grignard reagents let to lay aside this new reaction. However, some attempts were made to improve it, for instance by using allyl bromide (2) (3) instead of iodide : but, although allyl zinc bromides were recognized to be more active with nitriles than allyl magnesium bromides (4), the moderate to low yields generally observed made these reactions not very useful in organic synthesis (5). So, allylkétones and more generally β,γ-unsaturated ketones are usually obtained indirectly by long, tedious and rather sophisticated procedures (6).



We wish now to report an improvement of the Barbier reaction (8) by using zinc-silver couple (7) ; allylic bromides were then added to nitriles to afford β,γ-unsaturated ketones in high yields (see Table). The method is very simple and presents a real synthetic interest.



Preparation of the zinc-silver couple

To a stirred refluxing solution of silver acetate (100 mg) in glacial acetic acid (200 ml), coarse zinc powder (100 g) was added all at once and the mixture stirred for 30 secondes, and then quickly cooled. The zinc-silver couple so formed, was isolated by simple decantation, washed several times with anhydrous ether (6x100 ml) (it is necessary to remove all traces of acetic acid), dried under vacuum and finally stored at room temperature. Freshly prepared or several months old zinc-silver couples gave similar results.

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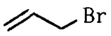
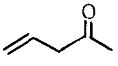
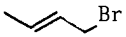
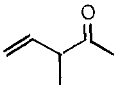
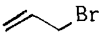
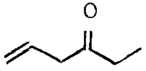
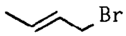
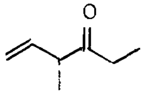
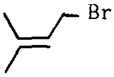
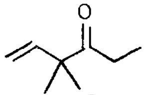
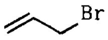
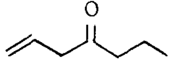
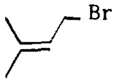
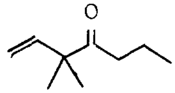
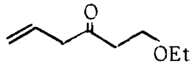
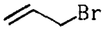
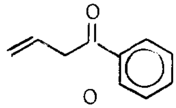
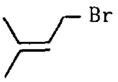
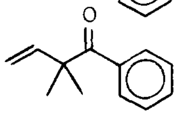
* Equipe de Recherche Associée au C.N.R.S.

Table : Preparation of β,γ-unsaturated ketones 1 - 10 from nitriles and allylic bromides in the presence of Zn/Ag couple

Nitrile	Bromide	Solvent	Ketone		(Yield)[a]	b.p.°C (mmHg)
CH_3CN		ether-THF (90:10)	1		(75%)[c]	108 (760)
-		benzene	2		(78%)[c]	111 (760)
CH_3CH_2CN		ether	3		(80%)[b]	125 (760)
-		benzene	4		(80%) [c]	77 (110)
-		THF	5		(71%)	79 (88)
$CH_3CH_2CH_2CN$		ether	6		(80%)[b]	86 (110)
-		THF	7		(68%)	102 (110)
$EtOCH_2CH_2CN$		ether	8		(78%)[b]	82 (17)
		benzene	9		(0%)[d]	-
-		THF	10		(67%)	71 (0.1)

a) Yield from nitrile of distilled product.

b) The presence of conjugated isomer was detected by glc (less than 4%).

c) No conjugated ketone was detected by glc.

d) Resinification occurred immediately.

Typical procedure : Preparation of 5-hexen-3-one 3

To a stirred mixture of propionitrile (11 g : 0.20 mole), dry ether (50 ml) and Zn/Ag couple (17.5 g ; 0.268 at.g.) was added dropwise 32.4 g (0.268 mole) of freshly distilled allyl bromide in order to maintain a slight reflux of ether (3 hours). When the addition was over, the mixture was stirred 10 h at room temperature, then pourred into a mixture of ice-water (100 g), saturated NH_4Cl solution (200 ml) and ether (100 ml). After 10 minutes of stirring the ether was decanted and the aqueous phase extracted with ether (2 x 100 ml). The combined organic phases were dried over Na_2SO_4 and distilled to give 14.7 g (b.p. 125°/760 mm Hg) (80%) of pure 5-hexen 3-one 3.

Remarks. The reactions were conducted in benzene or in tetrahydrofuran following the procedure reported for the ketone 3 ; an exothermic reaction was observed. Besides, with crotyl and isopropenyl bromides the addition was made within 6 h.

The use of a nitrogen atmosphere did not improve the yields. A concentration of 5 moles per liter was crucial since dilution led to lower yields. In the case of allyl bromide (9), the reaction took place in ether, benzene or THF with similar yields. In some cases with ether alone (preparation of 1 for example) the reaction was stopped by the formation of oily zinc salts coating the zinc dust (formation of pubbles). Such a drawback was not observed when the reaction was conducted in benzene or THF. Isopropenyl bromide led to very different results depending on the solvents used ; in ether a Wurtz reaction occurred mainly and low yields in ketones were obtained; the formation of ketones were improved in benzene and particularly in THF in which the Wurtz reaction was minor (10) ; for instance, the yields of the ketone 5 were of 30%, 56% and 71% in ether, benzene and THF, respectively.

From crotyl and isopropenyl bromides two products could be expected corresponding to an α or a γ attack. However as previously reported for crotyl bromide (4) (11), only the γ attack (the more substituted center) occurred.

The structures of the ketones 1 - 8, 10 were easily determined from their NMR, IR and mass spectra, in accordance with those already published(12). The ketones 1 - 8, 10 are stable ; after several months at room temperature, only the formation of a small amount of the conjugated isomer could be detected.

In conclusion, the reaction of nitriles with allyl bromides in the presence of zinc – silver couple is a very convenient way to β,γ-unsaturated ketones and even to certain α,β-unsaturated ketones, since the isomerization $\beta\gamma \longrightarrow \alpha\beta$ can be easily achieved by acids and bases. Some synthetic applications of this reaction will be published in a near future.

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6) A large number of preparations of β,γ-unsaturated ketones are known : For instance, allylketones : M.S. Newman and W.T. Both, J. Amer. Chem. Soc., 67, 154 (1945), V.A. Smit, A.V. Semenovskü, O.V. Lywbinskaya and V.F. Kucherov, Dokl, Akad. Nauk. SSR, 203, 604 (1972) ; R. Calas, J. Dunoguès, J.P. Pillot, C. Biran, F. Pisciotti and B. Arreguy, J. Organomet. Chem., 85, 149 (1975) ; M. Kosugi, Y. Shimizu and T. Migita, J. Organomet. Chem., 129, C36-38 (1977) ; S. Watanabe, T. Fujita, K. Suga, T. Inaba and M. Saida, Yakagaku, 28, 862 (1979).
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Ketones obtained by acylation of olefins : see the leading reference H.M.R. Hoffmann and T. Tsushima, J. Amer. Chem. Soc., 99, 6008 (1977).

7) J.M. Denis, C. Girard and J.M. Conia, Synthesis, 549 (1972).

8) For a review see : C. Blomberg and F.A. Hartog, Synthesis, 18 (1977).

9) Allyl chloride was unreactive.

10) The superiority of THF for the formation of organozinc compounds was recognized by Gaudemar (3).

11) C. Bouchoule and P. Miginiac, C. R. Acad. Sci., Série C, 266, 1614 (1968).

12) Ketones 5, 7 and 8 were still unknown ; satisfactory analyses were found for all of them.

5 : ^{1}H-NMR (CCl_4) δ (ppm) : 0.98 (t, J = 7 Hz, 3H) : 1.20 (s, 6H) ; 2.45 (q, J = 7 Hz, 2H), 5.15 (m, 2H), 6.00 (dd, 1H) : IR (neat) (cm^{-1}) : 3070, 2970, 1705 (ν C=O), 1625 (ν C=C) ; Mass : m/e 41, 57, 69, 126 (M^+).

7 : ^{1}H-NMR (CCl_4) δ (ppm) : 0.88 (t, J = 6 Hz, 3H), 1.20 (s, 6H), 1.55 (m, 2H), 2.40 (t, J = 7 Hz, 2H), 5.15 (m, 2H), 5.98 (dd, 1H) ; IR (neat) (cm^{-1}) : 3070, 2960, 1703 (ν C=O), 1625 (ν C=C) ; Mass : m/e 41, 43, 69, 71, 140 (M).

8 ^{1}H-NMR (CCl_4) δ (ppm) : 1.12 (t, J = 7 Hz, 3H), 2.56 (t, J = 6 Hz, 2H), 3.15 (m, 2H), 3.50 (2t, 4H), 4.85 to 6.35 (m, 3H) ; IR (neat) (cm^{-1}) : 3060, 2960, 2860, 1710 (ν C=O), 1630 (ν C=C), 1110 ; Mass : m/e : 41, 59, 69, 101, 142 (M^+).

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