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Graphite intercalation compounds as precursors of activated metals

II *. Synthesis of β,γ-unsaturated ketones through condensation of allylic organozinc derivatives with nitriles

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Abstract

Zinc supported on graphite (Zn^0/Gr) prepared from the binary KC_8 graphite intercalation compound was used as metallic reagent for the synthesis of various β,γ-unsaturated ketones from nitriles and a allylic halide. In aromatic series, the reaction is not influenced by the groups present on the ring of the nitrile. The most striking feature of the reaction is that the chloro and bromo parent reagents have comparable reactivities; this is attributed to the fact that the reaction of the activated organozinc derivative with the nitrile takes place on the surface of the carbonaceous support rather than in the solution.

Introduction

The organozinc derivatives used as reagents in organic synthesis at the end of the last century [1] were replaced by Grignard reagents [2]. Although the zinc compounds still found some applications in the preparation of ketones, they were soon replaced by organocadmium derivatives, which are readily obtained and give more consistent reactions [3]. However they proved to be useful in various reactions (Reformatsky, Simmons–Smith) when the metal was subjected to a specific activation, by ultrasound [4–7], combination with silver [8], use of dimethylformamide as solvent [10], comminution of the metal produced via the reduction of a zinc salt by potassium [11,12], or by treatment with the KC_8 graphitide [13–15].

In the particular case of the Barbier reaction in which we were interested, the reagents that have been recently used are zinc activated by silver [9], lithium, or the

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[*] Part I see ref. 20

zinc–silver couple activated by ultrasound [16,17]. The metals supported on graphite (M^0/Gr), which are obtained by reducing a metallic salt with the graphite intercalation compound KC_8 [18], show relatively good activity and selectivity in several reactions important in organic synthesis [19–24]. We therefore decided to investigate the use of zinc supported on graphite (Zn^0/Gr) and the condensation of allylic organozinc derivatives with nitriles for the direct synthesis of various β,γ-unsaturated ketones, which have usually to be prepared indirectly by long and tedious methods [25*].

Results and discussion

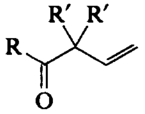
Zn^0/Gr was obtained, as in eq. 1, by treatment of one equivalent of anhydrous zinc chloride to with two equivalents of KC_8 in dry tetrahydrofuran.

$$2\,KC_8 + ZnCl_2 \longrightarrow 2\,KCl + ZnC_{16}\ (Zn^0/Gr) \qquad (1)$$

1. Experimental conditions

Optimum conditions were sought for the synthesis of 2,2-dimethyl-1-phenyl-3-butene-1-one by the reaction of 1-bromo-3-methyl-2-butene and benzonitrile with Zn^0/Gr in tetrahydrofuran (Eq. 2):

$$RCN + (R')_2C{=}CHCH_2X \xrightarrow[2)\ aq.\ NH_4Cl]{1)\ Zn^0/Gr,\ THF}$$



(2)

$(R = C_6H_5, R' = CH_3, X = Br)$

Under the optimum conditions described below, several kinds of graphitic supports, with various specific area and particles size, were tested. No important effect of the specific area was observed and high reactivity was obtained either with Lonza KS75 graphite (specific area 8 $m^2 \cdot g^{-1}$, particles diameter 75 μm) or natural Ceylon graphite (specific area < 1 $m^2 \cdot g^{-1}$, particles diameter 100–112 μm) which gave respectively 76 and 83% yields. However, with smaller particles of Ceylon graphite (40–63 μm, < 1 $m^2 \cdot g^{-1}$) the yield fell to 62%. During the first step of the process, we always noticed an agglomeration of the small flakes in the presence of liquid potassium, that led to an inhomogeneous KC_8 derivative.

All the comparative results presented below were obtained with Ceylon graphite (100–112 μm). After preliminary trials, the reaction times were fixed at 1 hour for the preparation of Zn^0/Gr and 5 hours for the condensation of the allylic organozincic derivative with the nitrile. With longer condensation times, the yield fell because of the decomposition of the β,γ-unsaturated ketone. The relative proportions of the reagents leading to an acceptable yield (83%) were (Zn)/(1-bromo-3-methyl-2-butene) = 1 and (1-bromo-3-methyl-2-butene)/(benzonitrile) = 2. With smaller amounts of benzonitrile, the yield decreased (72% for (1-bromo-3-methyl-2-butene)/(benzonitrile) = 1.3).

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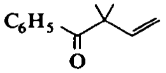
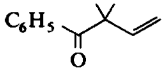
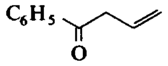
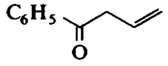
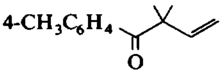
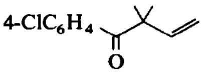
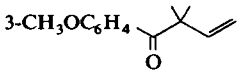
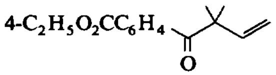
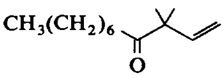
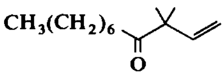
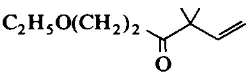
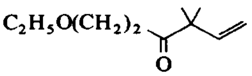
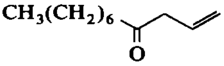
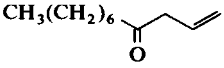
* Reference number with asterisk indicates a note in the list of references.

Table 1

Results of experiments performed with various nitriles and allyl halides.

No.	R	R′	X	Product	Yield (%)
1	C_6H_5	CH_3	Br		83[a]
2	C_6H_5	CH_3	Cl		87[a]
3	C_6H_5	H	Br		0[c]
4	C_6H_5	H	Cl		0[c]
5	$4\text{-}CH_3C_6H_4$	CH_3	Br		81[a]
6	$4\text{-}ClC_6H_4$	CH_3	Br		80[a]
7	$3\text{-}CH_3OC_6H_4$	CH_3	Br		85[a]
8	$4\text{-}C_2H_5O_2CC_6H_4$	CH_3	Br		81[a]
9	$CH_3(CH_2)_6$	CH_3	Br		53[a], 98[b]
10	$CH_3(CH_2)_6$	CH_3	Cl		72[a], 71[b]
11	$C_2H_5O(CH_2)_2$	CH_3	Br		57[a], 96[b]
12	$C_2H_5O(CH_2)_2$	CH_3	Cl		47[a], 69[b]
13	$CH_3(CH_2)_6$	H	Br		64[b,d]
14	$CH_3(CH_2)_6$	H	Cl		61[b,d]

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[a] Halide/Nitrile = 2. [b] Halide/Nitrile = 3. [c] A polymeric product was formed. [d] α, β conjugated ketone is also formed in this case.

2. *Application to the synthesis of various β,γ-unsaturated ketones (Table 1)*

When aryl nitriles were used, functional groups on the ring were not affected by the reaction, and the yields (80–85%) were not modified by their presence (reactions 5 to 8).

With similar proportions of reagents, the reactivity of 1-chloro-3-methyl-2-butene towards benzonitrile (reaction 2) was comparable to that of the bromo-derivative (reaction 1). This result is interesting since the chloro compounds do not react with the Zn/Ag couple [9]. Only with the Zn/Ag couple supported on graphite do bromo esters and chloro esters show comparable reactivities in the Reformatsky reaction [14,15].

We are not able to present relevant results for the reactions of benzonitrile with allyl bromide or allyl chloride since, a polymeric product was formed in both cases.

To obtain aliphatic ketones (reactions 9 to 14) in good yields, it was necessary to use a smaller amount of the nitrile: (1-halo-3-methyl-2-butene)/(nitrile) = 3 or (allyl halide)/(nitrile) = 3 (the halide being a chloride or a bromide). For instance, in the case of reaction 9, yields were 53% or 98% when the ratio (1-bromo-3-methyl-2-butene)/(heptyl cyanide) was 2 or 3, respectively. On the other hand, for reaction 10, the yield was not affected by a change in the relative amounts of reagents. As previously observed for the aromatic derivatives and also for reactions with heptyl cyanide, the reactivities of allyl bromide (reaction 13) and allyl chloride (reaction 14) were comparable. However, the β,γ-unsaturated ketone generated by reaction 13 or 14 readily isomerized to the α,β-conjugated ketone during the concentration of the medium before the purification by column chromatography, and lower yields were always obtained.

Conclusion

Zinc supported on graphite, prepared by the reduction of zinc chloride by KC_8, has a remarkable activity which permits its use as a source of allylic organozinc derivatives particularly efficient for condensations in the presence of nitriles.

With this reagent, the reactivities of bromo and chloro derivatives differ insignificantly for most of the nitriles studied. This unusual behaviour indicates that the organozinc derivative is activated by the graphite support. This indicates that the reaction with the nitrile occurs at the surface of the carbonaceous matrix rather than in the solution.

Experimental

General methods

TLC was performed on precoated silica gel plates (Merck 60 F_{254}) and flash chromatography on a silica gel column (Merck 40–63 μm). Gas-liquid chromatography was performed on a Girdel 300 chromatograph equipped with a flame ionization detector, using a 2.5 m column coated with 10% FFAP on chromosorb GAW DMCS.

^1H NMR spectra were recorded on a Varian EM 360 NMR spectrometer operating at 60 MHz with tetramethylsilane as internal standard. Infrared spectra were recorded on a FT-IR spectrometer Perkin Elmer model 1700 with films of the product on a NaCl plate.

Preparation of Zn^0/Gr

The supported metallic zinc (Zn^0/Gr) was prepared by the method described by Braga et al. [26]. The experiment is carried out under an argon flow. The graphite powder (3.1 g, 258 mmol) is dried at 150 ° C for 1 h. Small pieces of clean potassium (1.2 g, 30.69 mmol) are added and the mixture is vigorously stirred at 150 ° C for about 20 min until the characteristic golden colour of KC_8 is obtained. The solid is then cooled to 0 ° C and about 15ml of dry tetrahydrofuran (stored over phenanthrene radical anion) was distilled in-situ from KC_8 with the reactor kept at 0 ° C. Anhydrous zinc chloride in small excess (2.4 g, 17.6 mmol) stored under vacuum in an ampoule with a break-seal is dropped into the suspension after breaking of the seal with a magnetic rod. The mixture is vigorously stirred at 0 ° C for 10 min and for a further 50 min at 65 ° C (reflux of THF).

Synthesis and purification of β,γ-unsaturated ketones

This procedure is also carried out under an argon flow. The suspension prepared as above and containing Zn^0/Gr is cooled to 0 ° C. The nitrile derivative (7.67 or 5.12 mmol, respectively for allyl halide/nitrile = 2 or 3) is introduced directly into the reactor and the allyl halide (15.34 mmol) is introduced dropwise from a dropping funnel with vigorous stirring. The suspension is stirred for 5 h at room temperature. The mixture is then hydrolysed with a solution of concentrated NH_4Cl (25 ml). Diethyl ether (25 ml) is added and, after stirring, the suspension is filtered through a sintered glass plate. The organic phase is separated and the aqueous phase is washed twice with 10 ml of diethyl ether. The organic phase are collected and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the product is analysed by gas-liquid chromatography. The mixture is purified by flash chromatography on a silica gel column with a diethyl ether/petroleum ether (5/95) mixture as eluent. After evaporation of the solvent, the pure fractions isolated are weighted to determine the yield.

2,2-dimethyl-1-phenyl-3-butene-1-one

^1H NMR (CCl_4) δ(ppm): 1.35 (s, 6H); 5.12 (d, $J_{cis} = 10$ Hz, 1H); 5.15 (d, $J_{trans} = 18$ Hz, 1H); 6.17 (dd, $J_{cis} = 10$ Hz, $J_{trans} = 18$ Hz, 1H); 7.2 to 7.85 (m, 5H). IR (cm^{-1}): 3061, 2976, 1680 (C=O), 1635 (C=C).

2,2-dimethyl-1-(4-methyl phenyl)-3-butene-1-one

^1H NMR (CCl_4) δ(ppm): 1.34 (s, 6H); 2.30 (s, 3H); 5.10 (d, $J_{cis} = 12$ Hz, 1H); 5.10 (d, $J_{trans} = 19$ Hz, 1H); 6.17 (dd, $J_{cis} = 10$ Hz, $J_{trans} = 18$ Hz, 1H); 7.07 (d, 2H); 7.75 (d, 2H). IR (cm^{-1}): 3040, 2975, 1675 (C=O), 1610 (C=C).

2,2-dimethyl-1-(4-chloro phenyl)-3-butene-1-one

^1H NMR (CCl_4) δ(ppm): 1.30 (s, 6H); 5.15 (d, $J_{cis} = 10$ Hz, 1H); 5.15 (d, $J_{trans} = 18$ Hz, 1H); 6.15 (dd, $J_{cis} = 10$ Hz, $J_{trans} = 18$ Hz, 1H); 7.25 (d, 2H); 7.75 (d, 2H). IR (cm^{-1}): 3080, 2975, 1670 (C=O), 1640 (C=C).

2,2-dimethyl-1-(3-methoxy phenyl)-3-butene-1-one

^1H NMR (CCl_4) δ(ppm): 1.32 (s, 6H); 3.70 (s, 3H); 5.14 (d, $J_{cis} = 10$ Hz, 1H); 5.15 (d, $J_{trans} = 18$ Hz, 1H); 6.18 (dd, $J_{cis} = 10$ Hz, $J_{trans} = 18$ Hz, 1H); 6.7 to 7.5 (m, 4H). IR (cm^{-1}): 3082, 2973, 1679 (C=O), 1634 (C=C).

2,2-dimethyl-1-(4-carboethoxy phenyl)-3-butene-1-one

^{1}H NMR (CCl_4) δ(ppm): 1.25 (s, 6H); 1.25 (t, 3H); 4.3 (q, 2H); 5.15 (d, J_{cis} = 10 Hz, 1H); 5.15 (d, J_{trans} = 18 Hz, 1H); 6.15 (dd, J_{cis} = 10 Hz, J_{trans} = 18 Hz, 1H); 7.75 (d, 2H); 7.95 (d, 2H). IR (cm^{-1}): 3080, 2980, 1700 (C=O), 1640 (C=C).

3,3-dimethyl-1-undecene-4-one

^{1}H NMR ($CDCl_3$) δ(ppm): 0.85 (t, 3H); 1.20 (m, 16H); 2.40 (t, 2H); 4.98 (dd, J_{cis} = 10 Hz, J_{gem} = 1 Hz, 1H); 5.00 (d, J_{trans} = 17 Hz, 1H); 5.80 (dd, J_{cis} = 10 Hz, J_{trans} = 17 Hz, 1H). IR (cm^{-1}): 3080, 2960, 1700 (C=O), 1640 (C=C).

4,4-dimethyl-1-ethoxy-5-hexene-3-one

^{1}H NMR ($CDCl_3$) δ(ppm): 1.10 (t, 3H); 1.25 (s, 6H); 2.70 (t, 2H); 3.45 (q, 4H); 5.00 (dd, J_{cis} = 10 Hz, J_{gem} = 1 Hz, 1H); 5.05 (d, J_{trans} = 16 Hz, 1H); 5.80 (dd, J_{cis} = 10 Hz, J_{trans} = 16 Hz, 1H). IR (cm^{-1}): 3080, 2970, 1700 (C=O), 1640 (C=C).

1-undecene-4-one

^{1}H NMR ($CDCl_3$) δ(ppm): 1.25 (m, 13H); 2.39 (t, 2H); 3.10 (d, 2H); 4.92 (d, J_{cis} = 10 Hz, 1H); 4.97 (d, J_{trans} = 16 Hz, 1H); 5.75 (m, 1H). IR (cm^{-1}): 3070, 2960, 1700 (C=O), 1640 (C=C).

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