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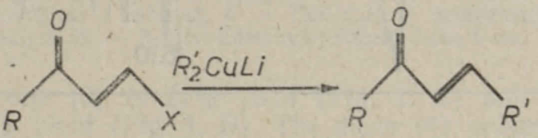
M. LOPP, L. GRUBER, Ü. LILLE

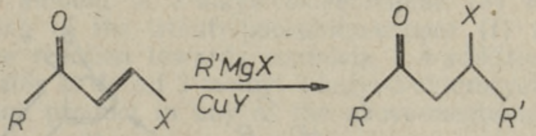
ALKYLATION OF A 2-ALKYL-3-CHLOROCYCLOPENT-2-ENE-1-ONE WITH GRIGNARD REAGENT AND WITH LITHIUM AND MAGNESIUM ALKYLCUPRATES

Alkylation of β-alkoxy-, β-alkylthio-, β-chloro- and β-iodovinyl ketones with lithium dialkylcuprates is known to give β-alkyl substituted unsaturated ketones [1–4].



X=-OAlk; -SAlk; -OAc; -Cl; J

Not long ago we demonstrated that β-alkyl-β-halogenoketone is one of the products gained in the additional reaction of Grignard reagent to aliphatic β-chloro- and β-iodovinyl ketones [5]. In the presence of one-valent ether-soluble copper complexes as catalysts, the above-mentioned reaction proceeds via 1,4-addition resulting in the formation of β-alkyl-β-halogenoketones mainly, depending on the reaction conditions [6].



X=Cl J , Y=J , $-C{\equiv}CH_7C_3$

In the present paper we report data obtained at the alkylation of 2-methyl-3-chlorocyclopent-2-ene-1-one (1) with Grignard reagent in the presence of a catalytic amount of one-valent copper complexes soluble in ether and with lithium dialkyl cuprates.

Discussion of results

Grignard reagents add to cycloenones in a 1, 2- or 1, 4-manner depending on the reaction conditions. In diethyl ether without using any catalysts, the 1, 4-addition reaction predominates [7]. The 3-chlorocyclopentenone (1) in reaction with ethylmagnesium bromide furnished a product which is characterized by an intensive absorption of OH-function at 3360 cm^{-1} and by a weak absorption at 1630—1705 cm^{-1} in the IR-spectrum

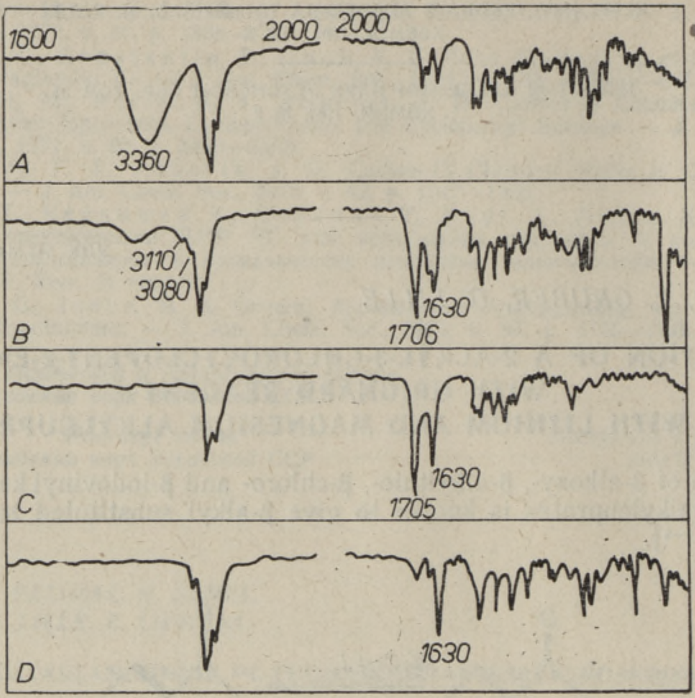
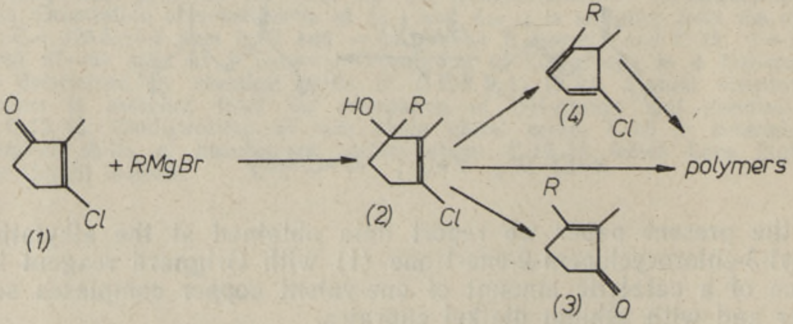


Fig. 1. IR-spectra of the products gained from the reaction between Grignard reagent and 2-methyl-3-chlorocyclopent-2-ene-1-one (1). *A* — crude product, *B* — product after spontaneous rearrangement, *C* — 2-methyl-3-ethylcyclopent-2-ene-1-one (3), *D* — 2-methyl-3-chloro-1-ethylcyclopenta-1, 3-diene (4).

(Fig. 1, *A*). This shows that the reaction occurs chiefly via 1, 2-addition with the formation of unsaturated alcohol (2). The resulting alcohol (2) is unstable and after the already known rearrangement the HCl is eliminated and β-alkylcyclopentenone (3) is formed [8, 9]. A part of the product is dehydrated, forming a diene (4) (Scheme 1). A transformation of alcohol (2) is observed in the IR-spectrum by the disappearance of OH-band absorption at 3360 cm^{-1} and by the appearance of new absorption lines at 1706, 1645 and 1630 cm^{-1} (Fig. 1, *B*). The transformation of the reaction product is accompanied by polymerization.



Scheme 1. The transformation of 2-methyl-3-chlorocyclopent-2-ene-1-one (1) in reaction with Grignard reagent.

From the obtained polymeric mixture we separated 2-methyl-3-ethyl-

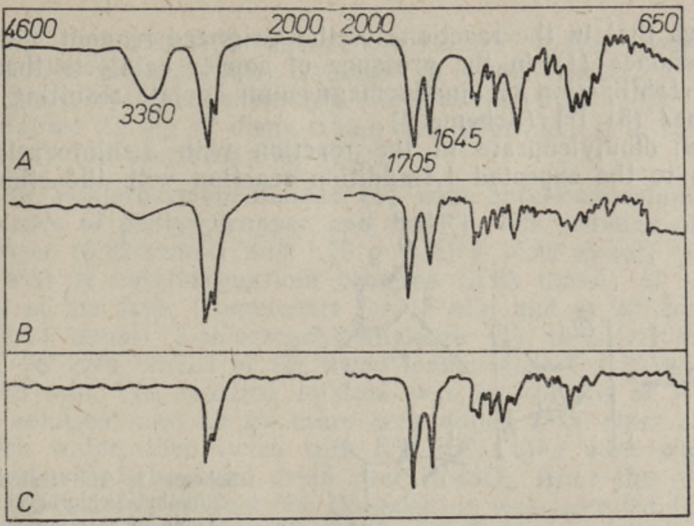
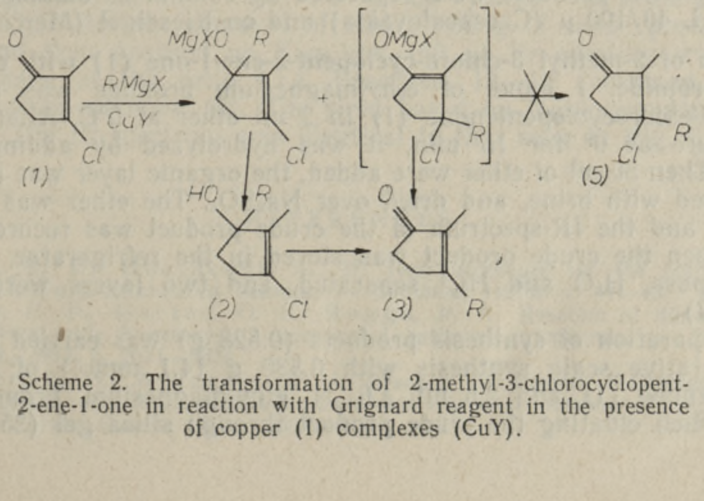


Fig. 2. IR-spectra of the products gained from the reaction between Grignard reagent and 2-methyl-3-chlorocyclopent-2-ene-1-one in the presence of copper(1) catalysts. *A* — HMPT: $C_3H_7C{\equiv}CCu$ (1 equivalent) as a catalyst, *B* — TBF·CuI (1 equivalent) as a catalyst, *C* — 3-butyl-2-methylcyclopent-2-ene-1-one.

cyclopent-2-ene-1-one (3) in 21% yield (Fig. 1, *C*) and a dienic compound (4) in 28% yield (Fig. 1, *D*). The diene (4) polymerizes rapidly. On adding hexamethylphosphorus triamide solubilized copper(I) pentyne (HMPT : $C_3H_7C{\equiv}CCu$ 2 : 1) to butylmagnesium bromide in the ratio 1 : 1, a mixture of 3-alkylcyclopentenone (3) and unsaturated alcohol (2) is formed (Fig. 2, *A*). The GLC analysis indicated that the ratio of alcohol (2) and 3-alkylcyclopentenone (3) is 1 : 1. The occurrence of the 1, 2-addition reaction, in spite of the presence of the copper catalyst, might be caused by the existence of different active alkylating particles in the reaction mixture, which react in different directions [10, 11].

When another catalyst of tributylphosphine-copper(I) iodide was applied [12], the amount of 3-alkylcyclopentenone (3) increased (Fig. 2,*B*). The doubling of the tributylphosphine-copper (I) iodide complex amount shifts the reaction towards complete 1, 4-addition.

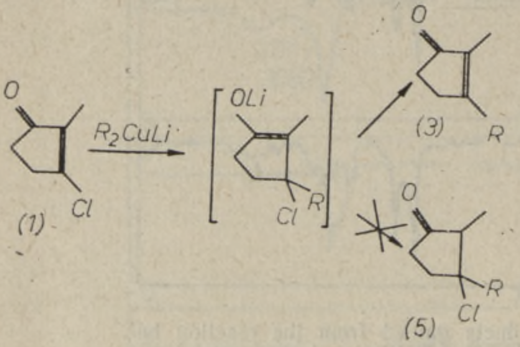
We were not able to detect 2-methyl-3-butyl-3-chlorocyclopentane-1-one (5) in the reaction product in any of the above-mentioned experiments.



Scheme 2. The transformation of 2-methyl-3-chlorocyclopent-2-ene-1-one in reaction with Grignard reagent in the presence of copper (1) complexes (CuY).

This shows that in the reactions of the Grignard reagent with 3-chlorocyclopentenones (1) in the presence of copper catalysts there was no expected stabilization of kinetic magnesium enolate resulting in β-halogenoketones (5) [6] (Scheme 2).

Lithium dibutylcuprate in the reaction with 3-chlorocyclopentenone (1) leads to the expected 1,4-addition reaction with the elimination of chlorine [1–4, 6]. The 3-alkylcyclopentenone (3) yield was 76% (Scheme 3). The order in which reagents were added did not have any effect on the composition of the reaction product.



Scheme 3. The transformation of 2-methyl-3-chlorocyclopent-2-ene-1-one in reaction with lithium dibutylcuprate.

Experimental

The experiments were carried out under argon atmosphere in a flame-dried apparatus. The ether was freshly distilled from CaH_2 before application. For low temperatures, the Dewar flask (CO_2-acetone) was used.

Using previously known methods we synthesized and analyzed tetrakis-/iodo(tri-*n*-butylphosphine)copper (I)/(TBF·CuI) [12], pentynylcopper ($C_3H_7C{\equiv}CCu$) [13], *n*-butyllithium [14]; hexamethylphosphorus triamide (HMPT) [15]; ethylmagnesium bromide and butylmagnesium bromide [16], 2-methyl-3-chlorocyclopent-2-ene-1-one [1, 17].

The amounts of different components in the reaction mixture were determined on the Võruchrom gas chromatograph with flame-ionization detector in the column 1 m 5% SE-30 on the Chromaton-N. The following spectrometers were used: IR Specord IR-71; NMR ^{13}C Brucker WH-90, at the Institute of Chemical and Biological Physics, Academy of Sciences of the Estonian SSR.

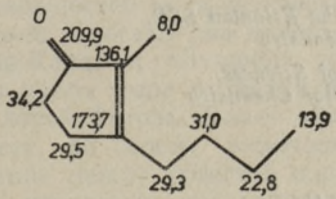
The reaction products were separated by column chromatography on silica gel L 40/100 μ (Czechoslovakia) and on Kieselgel (Merck).

Alkylation of 2-methyl 3-chloro-cyclopent-2-ene-1-one (1) with ethylmagnesium bromide. 1 mmol of ethylmagnesium bromide was added to 1 mmol 3-chlorocyclopentenone (1) in 2 ml ether at 0°C. After stirring the mixture at 0° for 15 min, it was hydrolyzed by adding NH_4Cl solution. Then 50 ml of ether were added, the organic layer was separated and washed with brine, and dried over Na_2SO_4. The ether was removed in vacuo, and the IR-spectrum of the crude product was recorded (Fig. 1, *A*). When the crude product was stored in the refrigerator, it began to decompose, H_2O and HCl separated, and two layers were formed (Fig. 1, *B*).

The separation of synthesis products (0.528 g) was carried out after the preparative scale synthesis with 0.530 g (4.1 mmol) of 3-chlorocyclopentanone (1) and 2.5 ml 1.6 N ethylmagnesium bromide (4.1 mmol). When eluating the crude product through silica gel (25 g) with a mixture of ethyl acetate/hexane at the ratio 1 : 4; the product partly decomposed. The fractions were collected in 7 ml. Fraction 4 contained 0.119 g of 3-alkylcyclopentenone (3) (IR-spectrum Fig. 1, *C*). Fractions 11—14 contained 21 mg of diene which was identified as a chlorocyclopentadiene (4) (IR-spectrum Fig. 1, *D*).

Alkylation of 3-chlorocyclopentenone (1) with butylmagnesium bromide in the presence of pentynylcopper and HMPT. The complex of 500 mg pentynylcopper (3.82 mmol) and 1.15 g HMPT (6.42 mmol) was added to 4.2 ml 0.91 N butylmagnesium bromide (3.83 mmol) at —78° and was stirred at the same temperature for 15 min and at 20° for 45 min. 483 mg (3.83 mmol) 3-chlorocyclopentenone (1) in 5 ml ether was added at —78° and stirred at the same temperature for 15 min and at —20° for 45 min. The reaction mixture was hydrolyzed at —20° with an NH_4Cl solution, and 50 ml ether was added. The ether layer was washed with water, then twice with 5% HCl, then with water, 10% $NaHCO_3$ and with brine, and dried over Na_2SO_4. After the removal of ether from the reaction product, the IR-spectrum was recorded (Fig. 2, *A*).

The reaction was repeated with 0.232 g of 3-chlorocyclopentenone (1) in 5 ml ether (1.78 mmol), 1.4 g TBF·CuI in 9 ml ether (3.55 mmol) and 3.9 ml 0.91 N C_4H_9MgBr (3.55 mmol), yielding 1.324 g of the crude product (Fig. 2, *B*) which, after purification on silica gel (40 g) by eluating with the mixture of ethyl acetate/hexane at the ratio 1 : 9, gave 0.165 g of 3-butylcyclopentenone (3). The yield based on 3-chlorocyclopentenone (1) was 60% (IR-spectrum Fig. 2, *C*). NMR ^{13}C-spectrum (tetramethylsilane as a standard):



Alkylation of 3-chlorocyclopentenone (1) with lithium dibutylcuprate. 1.452 g TBF·CuI in 15 ml ether (3.7 mmol) was added to 3.5 ml 2.08 N butyllithium (7.2 mmol) at —78° and stirred at the same temperature for 1 h. 383 mg of 3-chlorocyclopentenone (1) in 10 ml ether (3 mmol) were added to the reaction mixture and stirred at —78° for 1 h. The reaction mixture was hydrolyzed with an NH_4Cl solution and 50 ml ether was added. The ether layer was thrice washed with brine and dried over Na_2SO_4. After the removal of ether, 1.86 g of crude product were gained, and then purified on Kieselgel (40 g) by eluating with ethylacetate/hexane at the ratio 1 : 4. Fractions 13—18 contained 347 mg of 3-alkylcyclopentenone (3). The yield based on 3-chlorocyclopentenone was 76%. The IR-spectrum was identical to that seen in Fig. 2, *C*.

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Academy of Sciences of the Estonian SSR,
Institute of Chemistry

Hungarian Academy of Sciences,
Central Research Institute for Chemistry

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M. LOPP, L. GRUBER, Ü. LILLE

2-ALKÜÜL-3-KLOROTSÜKLOPENT-2-EEN-1-OONI ALKÜÜLIMINE GRIGNARD'I REAKTIIVI NING LIITIUM- JA MAGNEESIUMALKÜÜLKUPRAATIDEGA

Artikkel käsitleb 2-metüül-3-klorotsüklopent-2-een-1-ooni alküülimist etüül- ja butüülmagneesiumbromiidiga (eetris lahustuvate vask(I)-komplekside manulusel ja ilma nendeta) ning liitiumdibutüülkupraadiga. Toimub nii 1,2- kui ka 1,4-liitumine enoonsele süsteemile. Vask(I) katalüüsib 1,4-liitumist ja annab Grignard'i reaktiiviga liitudes 2-metüül-3-alküültsüklopent-2-een-1-ooni. Reaktsioonis ei toimu vahepealsete magneesiumienolaatide stabiliseerimist, elimineerub vesinikkloriid. Ka liitiumdialküülkupraadiga alküülimise tulemusena saadi 2-metüül-3-alküültsüklopent-2-een-1-oon.

М. ЛОПП, Л. ГРУБЕР, Ю. ЛИЛЛЕ

АЛКИЛИРОВАНИЕ 2-АЛКИЛ-3-ХЛОРЦИКЛОПЕНТ-2-ЕН-1-ОНА РЕАКТИВОМ ГРИНЬЯРА И АЛКИЛКУПРАТАМИ ЛИТИЯ И МАГНИЯ

Изучена реакция алкилирования 2-метил-3-хлорциклопент-2-ен-1-она бромистым этил- и бутилмагнием в присутствии растворимых в эфире комплексов одновалентной меди и без них, а также — дибутилкупратом лития. Показано, что без медных катализаторов в ходе реакции 1,2-присоединения образуются нестабильные еноляты, которые легко полимеризуются. В присутствии медных катализаторов в ходе реакции сопряженного 1,4-присоединения отщепляется хлористый водород и образуется 2,3-диалкилциклопент-2-ен-1-он. Это же соединение было получено при использовании диалкилкупратов лития.