METHYLENATION OF CARBONYL COMPOUNDS WITH METHYLENEDIMAGNESIUM IODIDE IN THE PRESENCE OF Et₂AlCl

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A method has been developed for the methylenation of carbonyl compounds with methylenedimagnesium iodide in the presence of Et_2AIC1 in 35-70% yield. In the presence of catalytic amounts of Ti and Pd complexes the yield of methylenation products is increased by 15-20%.

Mixed organometallic reagents derived from Ti-Al [1-4], Zr-Al [5], Zn-Al [6-8], Zn-Ti [6-10], and Zn-Cu [11, 12] are widely used for the olefination of aldehydes and ketones. Information on the use of organomagnesium compounds in these reactions is limited [13-15]. Thus, e.g., the methylenation of ketones with the Mg-CH₂I₂ reagent gives methylene alkanes in no more than 35% yield. The use of magnesium amalgam in those tests raises the product yield to 70% [13]. The relatively low yield of desired products and the use of metallic mercury reduce the preparative value of the magnesium reagents.

We hypothesized that when a Lewis acid capable of forming a complex was added to the methylenemagnesium reagent $(Mg-CH_2I_2)$, the stability of the methylenating reagent would be increased, and therefore the product yield. We studied the methylenation of cyclohexanone with $Mg-CH_2I_2$ in the presence of $SnCl_4$, $TiCl_4$, $AlCl_3$, R_nAlCl_{3-n} , $FeCl_3$, BF_3 , and other Lewis acids. We determined that the highest yields of methylenecyclohexane are obtained with simultaneous mixing of Mg, CH_2I_2 , and Et_2AlCl (2:1:2) in ether solution and subsequent addition of cyclohexanone to the reaction mixture.

The mechanism of methylenemagnesium iodide activation by Et_2AlCl is not at all clear. But the formation of a more active binuclear [16] magnesium-aluminum reagent (I) is not excluded; this would form in the diethyl ether solution as follows:



Indeed the ¹³C NMR spectrum of the complex shows a broadened δC^1 triplet at 1.49 ppm and a δC^2 quartet at 8.80 ppm. The broadening is ascribed to the quadrupole moment of the ²⁷Al nucleus. The triplet signal in the 0.28 ppm region corresponds to the C³ atom. The chemical shift of the carbon in CH₂(MgI)₂ is -6.3 ppm. The measured SSCC value (J₁₃C₃-1_H), 109.9 Hz, is typical [17] of the α carbons of organomagnesium compounds.

The reaction of complex (I) with an ether solution of cyclohexanone (30 min at 0°C, then 3 h at 25°C) gives methylenecyclohexane (II) in 65% yield. Replacement of Et_2AlCl by other organoaluminum compounds reduces the yield of (II) from 65 to 32% in the sequence $Et_2AlCl >$ $i-Bu_2AlCl > Et_3Al > i-Bu_3Al$. In these tests we noted 5 to 30% reduction of starting cyclohexanone to cyclohexanol. The solvent was ether or 1:1 ether—benzene. In hexane the yield of (II) is 35%, in THF it is 3 to 5%. In the absence of metallic magnesium the reaction does not go; replacement of CH_2I_2 by CH_2Br_2 reduces the yield of (II) to 30%. We were not able to obtain an active complex with CH_2Cl_2 .

Olefination of cyclic, alicyclic, or aromatic ketones or aldehydes with complex (I) gave the respective products (II)-(VIII) in 35-70% yields (Table 1).

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2350

| Compound | Methylenation products | Reaction time, h | Yield, % |
|--|--|---------------------|----------|
| ◯ =0 | $ = CH_2 (II) $ | 3 | 65 |
| $(n-C_4H_9)_2C=0$ | $(n-C_4H_9)_2C=CH_2$ (III) | 3.5 | 70 |
| $\sum = 0$ | $=CH_2$ (IV) | 3 | 60 |
| (n-C ₇ H ₁₅) ₂ C=0 | $(n-C_7H_{15})_2C=CH_2$ (V) | 3,5 | 45 |
| СНО | CH=CH ₂ | | |
| | | 4 | 40 |
| O ∥ PhCCH₃ | CH₂ ∥ PhCCH₃ (VII) | 4 | 35 |
| O ∥ PhCPh | CH ₂ PhCPh (VIII) | 4,5 | 35 |
| $\begin{array}{c} R \\ C = 0 + CH_2 \\ R' \end{array} \xrightarrow{M} \begin{array}{c} OM \\ \rightarrow CH_2 - C - R \rightarrow CH_2 = C \\ M \\ M \\ H' \\ R' \end{array} \xrightarrow{H} \begin{array}{c} R \\ R' \\ R' \end{array}$ | | | |

TABLE 1. Methylenation of Carbonyl Compounds with Magnesium-Aluminum Reagent (I) ($Et_2AlCl:Mg:CH_2I_2:ketone = 20:20:15:5$, ether)

When the reaction is carried out in the presence of catalytic amounts of the Cp_2TiCl_2 or Pd(Ph₃P)₂Cl₂ complexes, the yield of methylenation products is increased by 15-20%.

We attempted the olefination of cyclohexanone using phenyl- (IX) and benzyl-2,2-dibromocyclopropane (X) with Mg and Et_2AlCl . In the presence of catalytic amounts of FeCl₃, instead of the expected olefination product we obtained the substituted cyclopropanes (XI) and (XII) with high selectivity, at 100% conversion of the starting dibromocyclopropanes (IX) and (X).



Without a catalyst the reaction is less selective, and forms a 6:5:4 mixture of phenyl-2-bromocyclopropane, phenylcyclopropane, and phenylallene. Olefination of cyclohexanone using phenyl-2,2-dibromocyclopropane (IX) with $Pd(Ph_3P)_2Cl_2$ as catalyst, permits the reaction to be directed exclusively to the formation of phenyl-2-bromocyclopropane (XIII), with complete conversion of (IX). The reaction is of interest as a variant of the selective monoreduction of gem-dibromocyclopropanes [18].

EXPERIMENTAL

The reaction was carried out in an atmosphere of dry Ar. Ether was distilled from LiAlH₄ before use. GLC was carried out on a Khrom-5 unit in a current of He, column 1.2 m × 3 mm, 5% SE-30 on Chromatone N-AW. PMR spectra were obtained in CCl₄ with a Tesla BS-467 spectrometer (60 MHz); ¹³C NMR spectra, with a Jeol FX-90Q spectrometer with complete quenching of protons and "mono-resonance" in Et₂O relative to TMS. IR spectra were obtained with a UR-20 spectrometer (film). Mass spectra were obtained with a MKh-1306 spectrometer at 70 eV and 200°C.

<u>Olefination of Carbonyl Compounds.</u> (a). To a solution of 2.40 g (20 mmoles) of Et_2AlCl in 5 ml of ether was added 0.48 g (20 mmoles) of magnesium powder in an Ar current, then at 0-5°C 2.68 g (10 mmoles) of CH_2I_2 in 5 ml of ether dropwise. The mixture was stirred for ~15 min. After 30 min at 0°C 0.56 g (5 mmoles) of 3-methylcyclohexanone in 5 ml of ether was added and the mixture was stirred at room temperature for 3 h. Then at 0°C the reaction mixture was treated successively with saturated NH_4Cl solution and 5% HCl. The organic layer was separated, the aqueous layer was extracted with ether, and the combined organic layers were dried over MgSO₄. The yield of methylene 3-methylcyclohexane was determined by GLC using dodecane as internal standard.

(b). To 0.48 g (20 mmoles) of magnesium powder in 5 ml of ether in an Ar atmosphere at 0-5°C was added 2.40 g (20 mmoles) of Et_2AlCl , then dropwise 2.68 g (10 mmoles) of CH_2I_2 in 5 ml of ether. The mixture was stirred for ~15 min, then 0.078 g (0.3 mmole) of Cp_2TiCl_2 was added. After 30 min at 0°C 0.71 g (5 mmoles) of dibutyl ketone in 5 ml of ether was added. The reaction was carried out and the reaction mixture was worked up as indicated under (a) above.

(c). To a solution of 2.40 g (20 mmoles) of Et_2AlCl in 5 ml of ether in an Ar atmosphere was added 0.48 g (20 mmoles) of magnesium powder. At 0°C 0.081 g (0.5 mmole) of FeCl₃ was added, then dropwise 2.76 g (10 mmoles) of phenyl-2,2-dibromocyclopropane (IX) in 5 ml of ether. The mixture was stirred for ~15 min. After 30 min 0.49 g (5 mmoles) of cyclohexanone in 5 ml of ether was added, the mixture was stirred at room temperature for 5 h, then worked up as under (a) above. Phenylcyclopropane (XI) was obtained in ~80% yield, at ~100% conversion of the starting dibromide (IX). A similar result was obtained when the reaction was carried out without cyclohexanone. Under these conditions with catalysis by Pd (Ph₃P)₂Cl₂ (3 mole %) phenyl 2bromocyclopropane is formed in ~60% yield, with ~100% conversion of the starting phenyl-2,2dibromocyclopropane.

Compounds (II), (III), (V)-(VIII), (XI), (XII), and (XIII) were identified by comparison with the compounds described in [1, 12, 13, 19, 20].

Methylene-3-methylcyclohexane (IV), bp 44-45°C (30 mm), n_D^{23} 1.4435. IR spectrum (ν , cm⁻¹): 3082, 2940, 2880, 1655, 1450, 1120, 895. PMR spectrum (δ , ppm): 0.87 d (3H, CH₃, J = 4 Hz); 1.10-2.17 m (9H, CH, CH₂); 4.50 s (2H, CH₂=); M⁺ 110.

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