

COMPLEXES AND REACTIONS OF SUBSTITUTED MAGNESIUM AMIDES WITH ISOBUTYRIC ACID ESTERS

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Hexamethyldisilylaminomagnesium bromide and bis(hexamethyldisilylamino)magnesium form by reacting with methyl or tert-butyl isobutyrate either coordination complexes or products of Claisen condensation. The complexes thus obtained were isolated in the pure state and characterized by their infrared and NMR spectra.

Isobutyric acid esters substituted with a metal in the α -position represent in the first approximation models of reaction centres obtained in the anionic polymerization of methacrylic esters or also arising during the Claisen condensation of esters. Recently, esters of α -lithioisobutyric acid have been prepared advantageously^{1,2} by metalation of esters with lithium salts of secondary amines, and were successfully isolated in the pure state³. In our attempts to prepare analogous α -magnesium derivatives, hexamethyldisilylaminomagnesium bromide and bis(hexamethyldisilylamino)magnesium were used as the metalation agents, mainly because of their good solubility in nonpolar solvents and their branched structure which reduced the possibility of reaction of the agent with the carbonyl group. The above reactions did not lead to the goal we had in mind; instead, other products were isolated and characterized as coordination complexes of the reacting compounds. As yet, no similar compounds have been isolated in the pure state; since they are important for the explanation of the reaction mechanism of organomagnesium compounds, their properties were investigated in greater detail.

EXPERIMENTAL

All reactions and operations with organometallic compounds were performed in an argon atmosphere. The samples for analysis, IR and NMR spectra were dried 6 h at a pressure of 0.5 Torr at room temperature, if not given otherwise. The magnesium content was determined after hydrolysis by titration with sodium ethylenediaminetetraacetate; the nitrogen content was determined after Kjeldahl. The infrared spectra of the products were measured with a Perkin-Elmer 457 apparatus, mostly as 10% solutions in a CsJ cell 0.05 mm thick. The NMR spectra of benzene solutions were measured with a JEOL PS-100 apparatus at a frequency of 100 mc/s. The GLC analyses were performed with a Perkin-Elmer 112 E apparatus on a GE-XE-20% column on Chromosorb.

The solvents, methyl isobutyrate (*Ia*) and tert-butyl isobutyrate (*Ib*) and methyl ester of 3-oxo-2,2,4-trimethylpentanoic acid were dried with calcium hydride and rectified.

Hexamethyldisilylaminomagnesium bromide (*Ila*) was obtained by a reaction of hexamethyldisilazane with ethylmagnesium bromide. Bis(hexamethyldisilylamino)magnesium (*Ilb*) was obtained from *Ila* and sodium hexamethyldisilyl amide⁴. Methyl and tert-butyl α -lithioisobutyrate were obtained by metalation of the respective esters with N-lithium diisopropyl amide³. Tert-butoxymagnesium bromide was prepared by a reaction of ethylmagnesium bromide with tert-butyl alcohol and recrystallized from ether.

Complexes IIIa, IIIc and IIId. (Scheme 1). An equimolar amount of isobutyric acid ester was added dropwise to a saturated solution of *Ila* or *Ilb* in toluene at 0°. After half an hour at room temperature the toluene was evaporated *in vacuo* at 20°C, the residue was recrystallized twice from pentane at -70°C (complex *IIIc* crystallized directly from the reaction mixture), and the crystals thus obtained were dried *in vacuo* at 0°C. The yields and analytical data of complexes were as follows: *IIIa* 84%, for C₁₁H₂₈BrMgNO₂Si₂ (366.7) calculated: 6.66% Mg, 3.82% N; found: 6.47% Mg, 3.73% N; *IIIc* 74%, for C₁₄H₃₄BrMgNO₂Si₂ (408.8) calculated: 5.98% Mg, 3.43% N; found: 6.27% Mg, 3.52% N; *III d* 75%, for C₂₀H₅₂MgN₂O₂Si₄ (489.4) calculated: 4.97% Mg, 5.74% N; found: 4.55% Mg, 5.61% N.

Hydrolysis and acylation of complex IIIa. From a solution of 0.5 g of complex *IIIa* and 0.0701 g of cumene (internal standard) in 10 ml of toluene aliquots were taken for the hydrolysis with diluted (15%) H₂SO₄ at 0°C and for the acylation with isobutyryl chloride; the acylating mixture was hydrolyzed with diluted (15%) H₂SO₄ at room temperature after 12 h. In both cases, methyl isobutyrate (*Ia*) was determined (by GLC) in the reaction in an almost 100% yield.

Reaction of ester Ia with reagent Iib. Ester *Ia* (3.02 g, 29.5 mmol) was added to 10.15 g (29.5 mmol) of *Iib* in 20 ml of benzene while stirring at 0°C. After 5 h at room temperature benzene was evaporated *in vacuo* and the residue was crystallized from 15 ml of pentane at -70°C. The crystals thus obtained were recrystallized twice from the same solvent; 3.85 g (yield 50%) of colourless crystals of *IV* was obtained (Scheme 2). For C₂₁H₅₂MgN₂O₃Si₄ (517.3) calculated: 4.70% Mg, 5.43% N; found: 4.95% Mg, 5.32% N.

Thermal decomposition of IV. 3.5 g of *IV* was heated *in vacuo* at 90°C. The compound melted while yielding hexamethyldisilazane which was isolated and identified (infrared spectrum). The mixture which solidified again during heating for 10 h, was then crystallized from pentane and recrystallized from toluene at -70°C. Colourless crystals were dried *in vacuo* at 60°C; the yield was 2.0 g (83%) of *V* (Scheme 2). For C₁₅H₃₃MgNO₃Si₂ (355.9) calculated: 6.84% Mg, 3.94% N; found: 6.70% Mg, 4.06% N.

Hydrolysis of *IV* or *V* with diluted (15%) H₂SO₄ at 0°C gave rise to methyl ester of 3-oxo-2,2,4-trimethylpentanoic acid (*VIa*) in an amount of 80% or 90% theor. respectively by GLC.

Reaction of β -ketoester VIa with Iib. To a solution of 3.05 g (8.83 mmol) of *Iib* in 10 ml of pentane, 1.52 g (8.83 mmol) of β -ketoester *VIa* was added at 0°C, and the mixture was cooled to -70°C after 15 min at room temperature. The crystals obtained were filtered off, washed with pentane and dried. The yield was 3.5 g (77%) of *IV*. For C₂₁H₅₂MgN₂O₃Si₄ (517.3) calculated: 4.70% Mg, 5.43% N; found: 4.71% Mg, 5.51% N. The IR and NMR spectra of this product were identical with those of the compound isolated after the reaction of ester *Ia* with *Iib*, thus proving the structure of the latter.

Reaction of tert-butyl α -lithioisobutyrate (VIIb) with tert-butoxymagnesium bromide (VIII). To a solution of 5.33 g (35.5 mmol) of *VIIb* in 30 ml of tetrahydrofuran, a solution of 6.20 g (35.5 mmol) of *VIII* in 45 ml of tetrahydrofuran was added dropwise at -50°C. The mixture was heated to 25°C and the solvent evaporated *in vacuo* after 15 min. The residue was dissolved in 20 ml of benzene and the solution left to stand at room temperature for 24 h. After an hour a white precipitate appeared in the solution with a simultaneous separation of isobutylene (ac-

ording to the infrared spectrum). The precipitate was washed with tetrahydrofuran at 40°C and dried *in vacuo* at 60°C. The yield was 5.0 g (76%) of tert-butoxymagnesium isobutyrate (*X*). Infrared spectrum (nujol): 1 621 (s), 1 590 (s), 1 308 (m), 1 238 (s), 1 225 (m), 1 202 (s), 1 100 (w), 1 025 (w), 960 (s), 930 (m), 763 (m), 589 (s), 499 (s), 466 (w), 422 (w), 365 (w), 335 (w) cm^{-1} . For $\text{C}_8\text{H}_{16}\text{MgO}_3$ (184.5) calculated: 13.18% Mg; found: 13.00% Mg.

Hydrolysis of *X* with a diluted (50%) sulphuric acid in the pentane medium at -50°C yielded isobutyric acid, which was isolated by vacuum distillation in a 40% yield (identified by the infrared spectrum and GLC).

A mixture of *VIIb* and *VIII* after 64 h in tetrahydrofuran at room temperature yielded predominantly products of the Claisen condensation. Hydrolysis of the reaction mixture with dilute (50%) H_2SO_4 at -50°C gave rise to tert-butylester of 3-oxo-2,2,4-trimethylpentanoic acid (*VIb*) in a 41.5% yield; the product was distilled, b.p. 124–126°C/30 Torr and identified by GLC and the infrared spectrum.

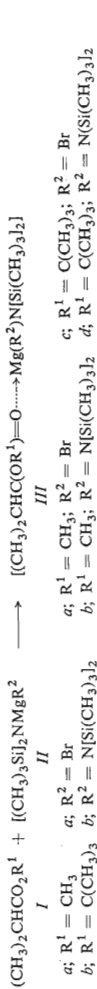
Reaction of lithium isobutyrate with VIII. To a suspension of 5.71 g (60.8 mmol) of lithium isobutyrate in 40 ml of tetrahydrofuran, a solution of 10.78 g (60.8 mmol) of *VIII* in 60 ml of tetrahydrofuran was added dropwise at -20°C. After 6 h of shaking the product was washed with the solvent at 40°C and dried *in vacuo* at 60°C. The yield was 9.3 g (83%) of salt (*X*). The infrared spectrum was identical with that of a product isolated from a reaction of *VIIb* with *VIII* in benzene. For $\text{C}_8\text{H}_{16}\text{MgO}_3$ (184.5) calculated: 13.18% Mg; found: 13.09% Mg.

Investigation of the rate of autocondensation of the product of reaction of methyl α -lithioisobutyrate (VIIa) with VIII. 0.6248 g (5.78 mmol) of (*VIIa*) and 0.5128 g of cumene (internal standard) were dissolved in 2.13 ml of tetrahydrofuran at 30°C, and a solution of 1.0248 g (5.78 mmol) of *VIII* in 6.5 ml of tetrahydrofuran was added immediately. Samples of the reaction mixture were taken at certain time intervals and injected into a mixture of acetic acid and tetrahydrofuran. After the precipitate had sedimented the clear solution was analyzed by GLC (the amount of esters *Ia* and *VIa* was determined). The autocondensation halftime of the reaction product of *VIIa* and *VIII* was one hour, while for *VIIa* alone the halftime was 22 h (ref.⁸).

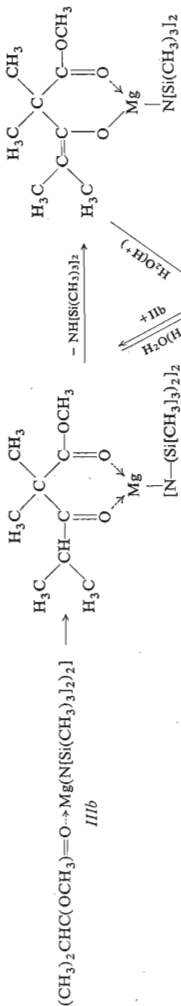
RESULTS AND DISCUSSION

Methyl isobutyrate (*Ia*) and tert-butyl isobutyrate (*Ib*) reacted with hexamethyldisilylaminomagnesium bromide (*Ila*) at room temperature in toluene while yielding coordination complexes *IIIa* and *IIIc*. A similar reaction was observed for bis(hexamethyldisilylamino)magnesium (*Ilb*) with tert-butyl isobutyrate (*Ib*) with formation of complex *III d* (Scheme 1). There was a good agreement between the structure of complexes proposed and the result of analysis, IR and NMR spectra, as well as with the hydrolysis with dilute sulphuric acid or acylation with isobutyryl chloride performed with complex *IIIa*.

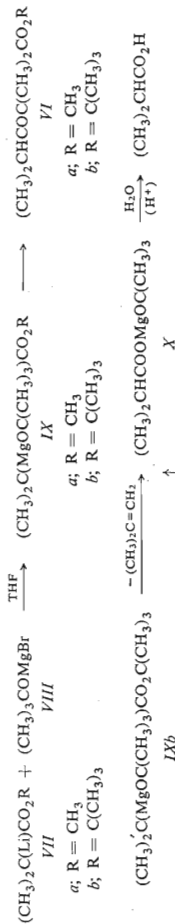
The infrared spectra of complexes (Table I) showed, in the region of valency vibration of the carbonyl group, a new intensive band with a lower frequency, besides the weak band of the carbonyl group of the original ester, which indicated the presence of traces of free ester due either to the dissociation or to the hydrolysis of the complex. A considerable decrease in the wave number of carbonyl bands compared to the carbonyl groups of the original esters *Ia* and *Ib* was caused by the coordination bond between the oxygen atom of the carbonyl group and the magnesium atom.



SCHEME 1



SCHEME 2



SCHEME 3

TABLE I
NMR and Infrared Spectra of Compounds I-VI

Compound	Wave number, cm^{-1}		Chemical shift ^b , τ				
	C=O	(O=C)O ^d	CH_3Si^c	$(\text{CH}_3)_2\text{C}^e$	$(\text{CH}_3)_2\text{CH}^d$	$(\text{CH}_3)_2\text{CH}^e$	$\text{R}^1\text{O}^e, \theta$
Ia	1 740 (s)	1 268 (m)	—	—	9.03	7.70	6.66
Ib	1 729 (s)	1 280 (m)	—	—	9.02	7.76	8.70
IIIa	1 736 (w)	1 318 (s)	9.71	—	9.11	7.61	6.65
IIIc	1 728 (w)	1 348 (m)	9.71	—	9.06	7.27	8.82
IIId	1 730 (w)	1 350 (m)	9.82	—	9.14	7.58	8.90
IV	1 720 (s)	1 310 (w)	9.71	9.08	9.28 ^f	7.75	6.83
V	1 668 (s)	1 305 (s)	9.80	8.51	—	—	6.77
	1 640 (m)					8.22 8.46	
VIa	1 744 (s)	1 270 (s)	—	8.80	9.11	7.40	6.66
	1 715 (s)						

^a Band in the region of combination vibrations of the (O=C)O bond. ^b p.p.m. from TMS. ^c Singlet. ^d Doublet. ^e Septet. ^f $J_{\text{cc}} = 6.5$ Hz, in the other cases $J_{\text{cc}} = 7$ Hz. ^g For the meaning of R¹ see Scheme 1 or 2.

A shift of the band of the $(\text{O}=\text{C})\text{—O}$ bond of the ester toward higher wave numbers was also in accordance with the existence of such a coordination bond. Analogous changes have already been described for spectra of the coordination complexes of carboxylic acids esters with halides of transition metals⁵ or with organometallic compounds⁶.

Another proof for the structure of complexes was provided by their NMR spectra (Table I) in which, besides the singlet of the $(\text{CH}_3)_3\text{Si}$ -groups, all the other chemical shifts observed in the NMR spectra of the original esters *Ia* and *Ib* were also present. At the same time, the NMR spectrum ruled out alternative structures, such as α -magnesium esters of isobutyric acid, in the NMR spectra of which only singlet bands ought to be found, because of the absence of the methin proton.

The coordination complexes were crystalline hygroscopic compounds, readily soluble in nonpolar solvents (pentane *etc.*). Their stability was low, so that already after standing for several hours at room temperature or immediately on heating to 60°C *in vacuo* decomposition took place. The decomposition products were complex mixtures of compounds which we could not separate without hydrolysis.

Bis(hexamethyldisilylamino)magnesium (*Iib*) yielded with methyl isobutyrate (*Ia*) in toluene at room temperature the corresponding coordination complex *IIIb*, which immediately reacted further *via* Claisen condensation and gave rise to product *IV*. Compound *IV* exhibited good stability in the isolated state at room temperature, but on heating to 90°C *in vacuo* decomposed while yielding hexamethyldisilazane and compound *V* (Scheme 2). Compound *IV* was also obtained by another route, namely by a reaction of the methyl ester of 3-oxo-2,2,4-trimethylpentanoic acid (*VIa*) with *Iib* in pentane.

The infrared spectrum of complex *IV* exhibited in the region of the carbonyl vibration a single intensive band at 1720 cm^{-1} , assigned to the carbonyl groups of β -ketoester coordinated to the magnesium atom. At the same time, in the region of $(\text{O}=\text{C})\text{—O}$ bond vibrations a shift by 40 cm^{-1} to higher wave numbers was observed, compared with the analogous band of the β -ketoester *VIa*. Besides the singlet of the $(\text{CH}_3)_3\text{Si}$ groups, the NMR spectrum of complex *IV* contained all bands present in the NMR spectrum of β -ketoester *VIa*, thus indicating its presence in the complex.

The infrared spectrum of compound *V* exhibited in the region of valency vibrations of the $\text{C}=\text{O}$ and $\text{C}=\text{C}$ bonds an intensive band at 1668 cm^{-1} and a medium intensive inflexion at 1640 cm^{-1} . In the NMR spectrum of this compound the three-proton singlets at 8.22 and 8.46 τ indicated the presence of two nonequivalent methyl groups. Both chemical shifts were ascribed to the methyl groups bonded to the exocyclic double bond. The best agreement with both the hydrolysis of the compound under investigation and its spectra was found for the chelate structure *V*; the other alternative structures were regarded as less probable.

The existence of complex *IIIb*, formed intermediately during a reaction between

ester *Ia* and *Iib*, was proved by the infrared spectrum of the reaction mixture recorded immediately on mixing the starting components and exhibiting — apart from other bands — also an intensive band near 1680 cm^{-1} , similarly as was found for complex *IIIa*. The intensity of this band decreased with time while a new band was formed at 1720 cm^{-1} , obviously corresponding to the carbonyl groups of compound *IV*. The greater stability of the complex of tert-butyl ester *IIIc* compared to the complex of the methyl ester *IIIb* can be explained by a weaker disposition of the tert-butyl esters towards a nucleophilic attack^{7,8}.

The isolation of coordination complexes supports the generally assumed reaction mechanism of the Grignard reagents with carbonyl compounds, according to which the first reaction step is an interaction of the reagent with the oxygen atom of the carbonyl group. Similar complexes of esters with the Grignard reagents have not been isolated in the pure state so far, mainly because of their short lifetime⁹.

It follows from the above results that by treating isobutyric acid esters with substituted magnesium amides no α -magnesium derivatives of the former could be obtained, in contrast with analogous lithium compounds. The success in preparing α -metalated esters by this method depends on the ratio of the metalation rate to the rates of the consecutive reactions of the α -metalated ester. This ratio is obviously less favourable for magnesium derivatives than for those of lithium. The above assumption was corroborated by determining the rate of autocondensation of methyl α -tert-butoxy-magnesium isobutyrate (*IXa*) in tetrahydrofuran obtained *in situ* from methyl α -lithioisobutyrate (*VIIa*) and tert-butoxymagnesium bromide (*VIII*), for which the rate of autocondensation was found to be 22 times higher than for methyl α -lithioisobutyrate alone. On the basis of different electronegativity of metals it can be assumed that the metalation abilities of organomagnesium compounds are generally lower compared to the organolithium derivatives.

According to other experiments carried out by us, the reaction of α -lithioisobutyric esters with alkoxy-magnesium bromide led most likely to the expected α -magnesium esters of type *IX* (Scheme 3), but their isolation was complicated by lithium bromide formed which could not be fully removed. Further unfavourable reactions that were operative here were the consecutive reactions of α -magnesium esters, namely, the autocondensation mentioned above and the elimination of isobutylene from tert-butyl α -tert-butoxy-magnesiumisobutyrate, which was predominantly observed in the hydrocarbon medium. tert-Butoxymagnesium isobutyrate (*X*) was isolated as the reaction product of β -elimination; its structure was confirmed by comparison with an authentic sample. Here again the phenomenon already recorded for α -lithioesters was observed³, namely, that autocondensation proceeds much slower in the hydrocarbon medium than in the tetrahydrofuran solution. This is obviously the reason why β -elimination could assert itself to a greater extent.

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