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ON THE STERIC COURSE OF ADDITION OF 1-LITHIO- AND 1-MAGNESIO-2-PIVALOYL-1,2,3,4-TETRAHYDROISOQUINOLINE TO ALDEHYDES AND KETONES. AN X-RAY CRYSTAL STRUCTURE DETERMINATION OF THE ORGANOMAGNESIUM REAGENT

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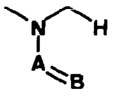
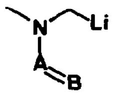
Summary

The steric course of the diastereoselective addition of the 1-bromomagnesium derivative **2** of *N*-pivaloyl-tetrahydroisoquinoline (THIQ) to acetophenone is proved by X-ray crystal structure analysis of the major product 1-(α-hydroxy-α-methylbenzyl)-2-pivaloyl-1,2,3,4-tetrahydroisoquinoline (**4**) to be the same as that for aldehydes (relative topicity *ul*, configuration of the adducts *u*). The reaction is much less selective if the lithiated reagent is employed. The crystal structure of the magnesium reagent (**2**) was determined. As crystallized from THF, **2** is monomeric, with an octahedrally coordinated Mg with three THF oxygens, the THIQ carbon, the pivaloyl oxygen and a bromine as ligands. A mechanistic proposal derived from the crystal structure explains both the higher selectivity observed with the Mg derivative and the fact that the *u*-diastereomer is formed preferentially.

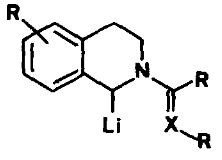
The lithiation of *N*-functionalized secondary amines **A** to give the nucleophilic aminoalkylating reagents **B** (d^1-reactivity [1]) is part of a useful method [2,3] of elaborating the structures of amines, and thus of synthesizing alkaloids.



A



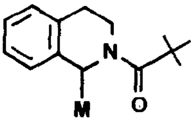
B



C

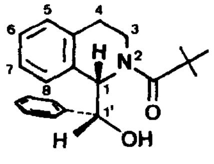
An especially interesting class **C** of reagents of this type is derived from tetrahydroisoquinolines (THIQ) [2,4–8]. Through certain chiral, non-racemic activators, the THIQ skeleton can thus be alkylated with a high degree of enantioselectivity [8], while additions of such reagents to aldehydes proceed with poor diastereoselectivity [5,7]. Recently we have shown that by changing the metal from lithium to magnesium almost complete diastereoselection can be achieved in hydroxyalkylations of a THIQ derivative [9,10].

Thus, the lithiated pivalamide **1** combines with benzaldehyde to give the diastereomeric adducts *l*-**3** and *u*-**3** [11] in a ratio of ca. 1/3. After transmetalation to the magnesium derivative **2** (by addition of $MgBr_2 \cdot$ etherate), the *u*-diastereomer is the sole product. This increase in selectivity also applies to other aromatic, as well as to aliphatic aldehydes and to certain ketones. The relative configuration of the hydroxyamides **3** was assigned by NMR spectroscopy and by chemical transformations [10]. Thus the vicinal coupling constants between the protons on C(1) and C(1′) of the isomers fit well with the values calculated from the dihedral angles [12], assuming a conformation with a hydrogen bond between the OH and the neighbouring C=O group. The assignment is confirmed by NMR comparison with similar THIQ derivatives of known configuration [13]. Typically, the aromatic hydrogens on C(8) of the *l*-diastereomers appear at high field due to shielding by the benzene ring in the 1′-position. In contrast to the compounds of type **3** obtained with aldehydes, the major product **4** (96/4) from the Mg reagent **2** and acetophenone appeared to have the *l*-configuration according to this characteristic upfield shift of the C(8) proton. However, rather than having the opposite configuration, the preferred conformation around the C(1)–C(1′) bond might have changed due to the additional methyl substitution. This is indeed the case: we were able to obtain suitable single crystals of the major diastereomer, and determined the molecular structure by X-ray crystallography (see Fig. 1 and Experimental section). Like the aldehyde adduct **3**, the main isomer **4** has *u*-configuration, and in both cases the relative topicity [11] with which the new C,C bond is formed is specified by *ul*, see **D**.

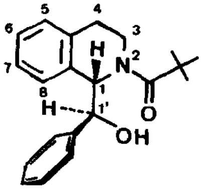


1 : M = Li

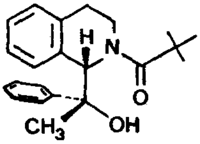
2 : M = Mg



u-3

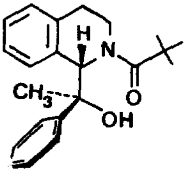


l-3

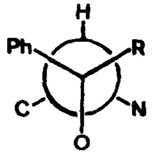


u-4

96:4
from
2 and
acetophenone



l-4

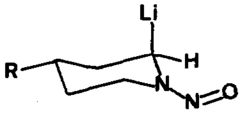


(rel. topicity *ul*)

D

With the product configuration established, two interesting questions arise: (a) why is the magnesium derivative the more stereoselective reagent?, and (b) why does the reaction take place preferentially with relative topicity *ul*? Unfortunately, no reliable information is available on the structures of organometallic reagents of type

B. From product configurations, it was concluded that in lithiated nitrosoamines the metal is located above the π-plane, see **5**, whereas in lithiated amides (such as **1** or **2**), the metal is supposed to be σ-bonded, see **6** [14–20]. In order to discuss the above questions with greater confidence we attempted to isolate single crystals of a metalated THIQ amide. We obtained suitable crystals of the magnesium derivative which had the composition (**2** · 3THF), also determined by elemental analysis and by



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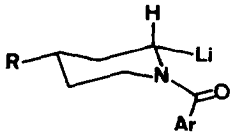

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deuterolysis of the crystals in an NMR tube and subsequent measurement. Crystals of the lithiated THIQ amide were also isolated and shown to have the composition

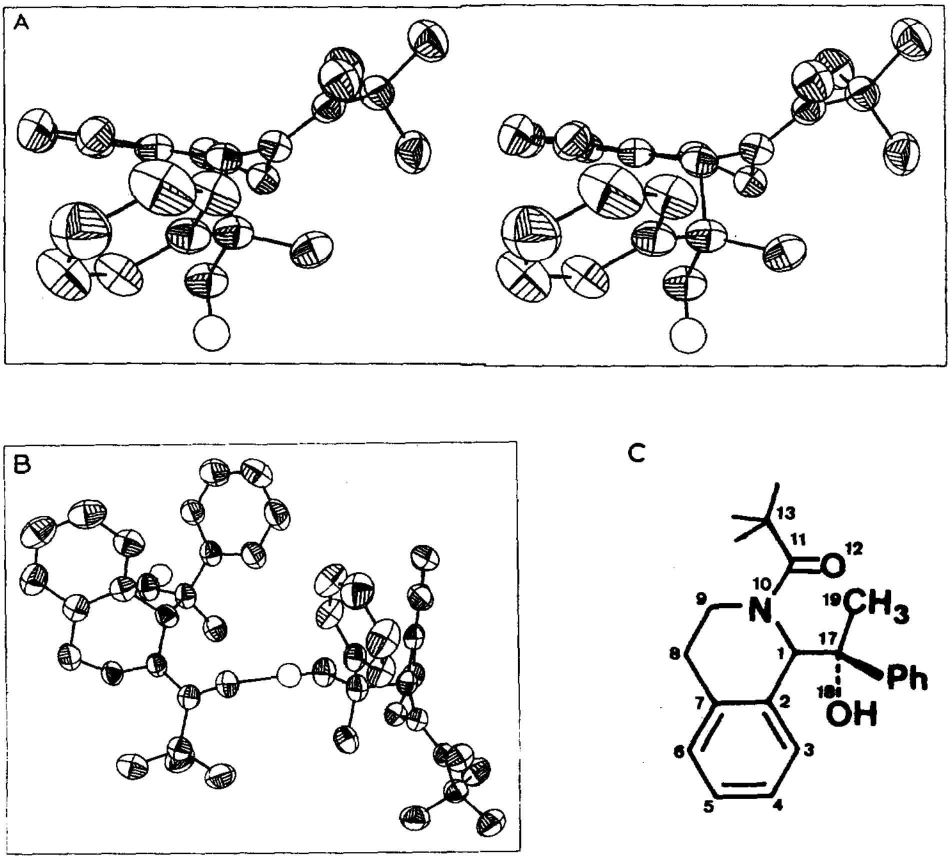


Fig. 1. A: Stereoview of an ORTEP plot of *u*-**4** as located in the crystal. The OH group and the C=O group do not form an intramolecular hydrogen bond. **B**: Dimeric unit of two *u*-**4**-molecules from the crystal packing lattice showing the intermolecular hydrogen bond. C: Numbering of the atoms of **4** in the X-ray structure determination.

(**1** · 2THF). To ascertain the identity of the crystalline material with the species normally present in solution, the crystals of **2** as well as their solution in THF was allowed to react with benzaldehyde. In both cases, this furnished the same product *u*-**3** obtained under standard experimental conditions [9,10].

The molecular structure of **2**, see Fig. 2, shows the metal to be in a pseudo-equatorial position of the THIQ ring system, and to be σ-bonded to its C(1) carbon atom. Intramolecular complexation by the carbonyl oxygen to give a planar five-membered ring is observed, and magnesium is further coordinated by a bromide and three THF molecules, and as expected the bromide occupies the position *trans* to the most electronegative ligand on the metal, the carbonyl oxygen. Magnesium halides and complexes thereof also show an octahedral coordination, whereas organomagnesium halides complexes with THF are normally monomeric species with four- or five-fold coordination of the metal [21]. In less polar solvents these compounds are known to be more highly aggregated. A further feature emerging from the structure of **2** pertains to the discussion of whether such compounds should be considered as intramolecularly chelated α′-metalated amides **7** or, as proposed by Beak [3,19,22,23], as derivatives of dipole-stabilized carbanions **8**. In the latter case we expect a

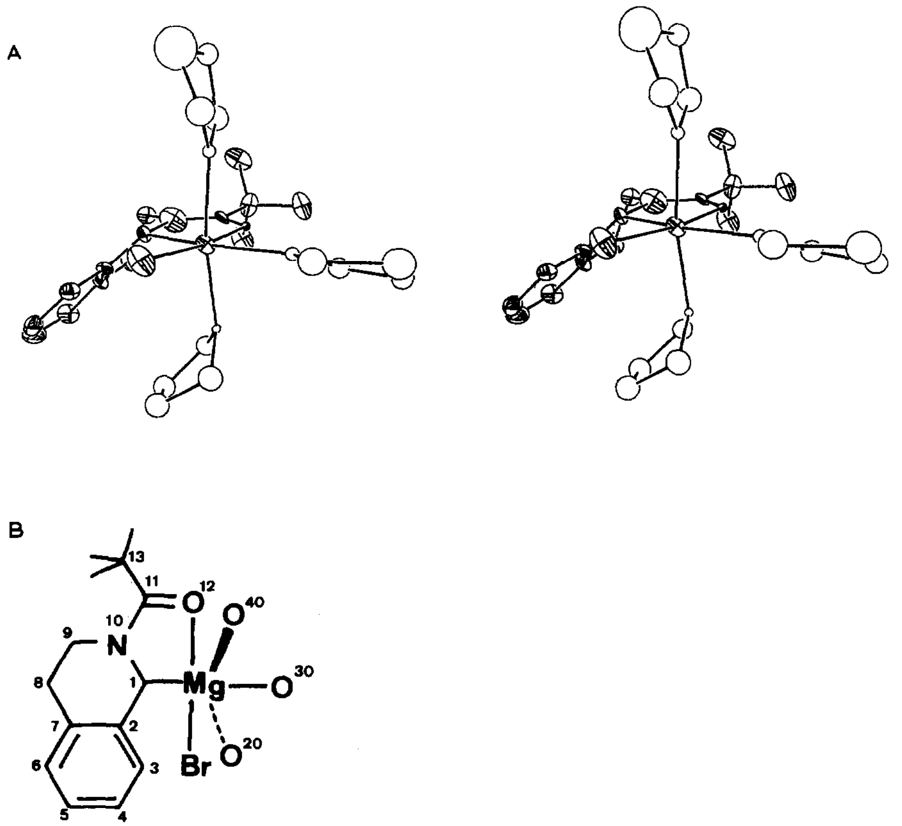
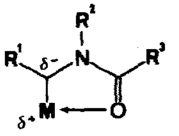


Fig. 2. A: Stereoview of an ORTEP plot of **2**. B: Numbering of the atoms in the X-ray structure determination.



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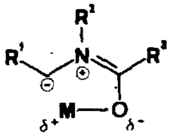

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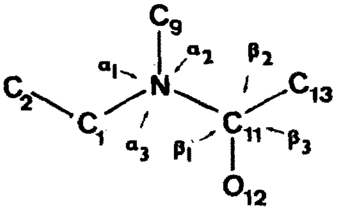
shortening of the C–N bond and a lengthening of the C=O bond as compared to ordinary amides, but as can be seen from Table 1, no significant deviation is found between the magnesium derivative **2** and the "simple" amide *u*-**4**. Likewise no such deviations are seen by comparison with standard values for amides [24] or magnesium complexes of amides [25]. We therefore consider **7** to be the more appropriate description of these and other similar organometallic derivatives. It is noteworthy that the absence of an effect of metalation on bond lengths and bond angles in the crystal structures described here appears to agree with the results of calculations [17], but is in contrast to the considerable changes (10–40 cm^{-1}) of the carbonyl and imine IR frequencies observed upon complexation with butyllithium, and even more so upon α′-lithiation [26,27].

We are now in a better position to discuss the questions raised above. First, the following general assumptions must be made: (a) The displacement of the metal in the reaction with an electrophile takes place with overall retention [28]. (b) The incoming carbonyl compound displaces a solvent molecule to form a complex with the metal in an initial step (see **9a**); such complexation of lithium and magnesium to lone pairs of carbonyl groups is known from X-ray structure analyses [25,29,30], the metal lying almost in the carbonyl plane and at an angle of less than 180° (non-linear complexation) and IR [26,27] and NMR measurements [31] also confirm this type of complexation in solution. (c) Of the three THF positions on the magnesium atom of **2**, the "*exo*"-position is most favorable for bonding and subsequent reaction of the electrophile; it is noteworthy that the Mg–O distance in

TABLE 1

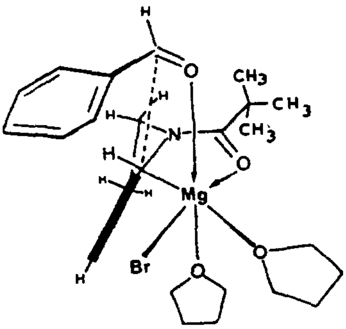
COMPARISON OF BOND LENGTHS (Å) AND BOND ANGLES (°) IN THE AMIDE POSITIONS OF THE MAGNESIO-THIQ DERIVATIVE 2 AND THE AMIDE *u*-4



Bond	C(1)–C(2)	C(1)–N	C(9)–N	N–C(11)	C(11)–O(12)	C(11)–C(13)
2	1.491(15)	1.482(13)	1.515(15)	1.365(14)	1.225(14)	1.547(17)
u-4	1.518(5)	1.472(4)	1.472(4)	1.355(4)	1.234(4)	1.541(5)
Angle	$α_1$	$α_2$	$α_3$	$β_1$	$β_2$	$β_3$
2	115.6(8)	126.1(9)	117.9(9)	119.5(10)	120.8(10)	119.7(10)
u-4	113.7(3)	127.6(3)	118.6(3)	119.7(3)	121.1(3)	119.2(3)

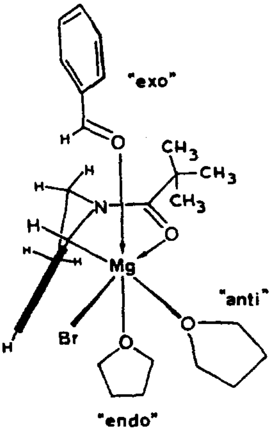
this position is the longest in the crystal structure of **2**, suggesting that the "*exo*"-THF molecule is easiest to replace.

Once the arrangement pictured by **9a** has been attained, the carbonyl compound can move over to form the new C,C bond with relative topicity *lk* (**9c**) or *ul* (**9b**). As a result of steric interaction of the phenyl substituent with a pivaloyl methyl group, the approach **9c** appears to be less favorable than **9b**, resulting in a *ul*-approach, as observed experimentally. In connection with the much higher diastereoselectivity of the reaction of the magnesium compound **2** as opposed to the lithium compound **1** it is relevant to compare the coordination spheres of these two metals: whereas with lithium one mostly finds four-fold (tetrahedral) coordination [29,30], the magnesium complex **2** has octahedral geometry, which brings the ligands closer together, angles of ca. 109 vs. ca. 90° (see **10** vs. **11**), while the bond lengths Mg–O/Mg–C vs. Li–O/Li–C do not differ significantly [21,29,30]. This means that in the case of the magnesium reagent the reacting complex is more crowded, the electrophile undergoing steric repulsions more strongly and earlier on the way to the transition state than in the case of the corresponding lithium compound. This should render the reaction more selective with the magnesium derivative.

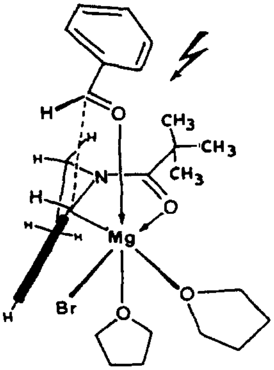


ul

9b

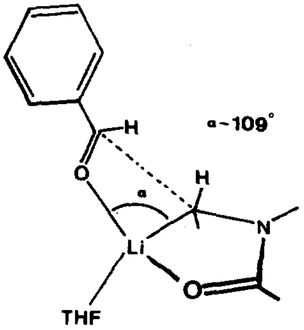


9a



lk

9c



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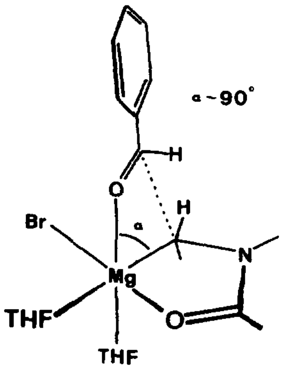

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Through knowledge of the molecular structure of a useful synthetic reagent we have thus been able to propose a reasonable explanation for both the sense as well as the degree of diastereoselectivity observed in its reactions. We will attempt to make use of this knowledge to design further synthetic applications of this and other organometallic reagents. While well aware of the fact that extrapolation from the crystalline state to the solution may not be wholly reliable [32,33], we believe that this way of elucidating mechanisms will supplement purely empirical optimizations of reaction conditions.

(Continued on p. 10)

TABLE 2

FRACTIONAL ATOMIC COORDINATES ($\times 10^4$) in **2**

Atom	x	y	z
Br	7469(1)	1851(1)	8196(0)
Mg	7906(3)	4154(3)	7791(3)
C(1)	6984(8)	4513(9)	6790(5)
C(2)	6961(9)	3742(10)	6097(6)
C(3)	6906(9)	2424(11)	6162(6)
C(4)	6926(9)	1639(13)	5550(7)
C(5)	6997(10)	2155(14)	4835(8)
C(6)	7071(11)	3458(13)	4751(7)
C(7)	7025(8)	4259(11)	5385(6)
C(8)	7057(9)	5654(11)	5285(6)
C(9)	6575(9)	6350(12)	5946(7)
N(10)	7091(7)	5875(8)	6632(5)
C(11)	7713(8)	6549(10)	7062(7)
O(12)	8142(5)	6022(7)	7568(4)
C(13)	7874(10)	7971(12)	6923(7)
C(14)	8342(10)	8235(12)	6163(7)
C(15)	6944(10)	8756(12)	7046(7)
C(16)	8614(10)	8408(10)	7504(7)
O(20)	9155(5)	3602(7)	7176(4)
C(21)	9361(8)	4051(10)	6440(6)
C(22)	9408(8)	2850(9)	5939(6)
C(23)	9446(8)	1742(10)	6486(6)
C(24)	9632(8)	2409(11)	7235(6)
O(30)	8936(5)	4400(7)	8658(4)
C(31)	9669(14)	5334(18)	8609(12)
C(32)	10346(14)	5246(19)	9246(11)
C(33)	9905(17)	4125(21)	9794(14)
C(34)	9101(16)	3383(22)	9291(13)
C(36)	9859(15)	5040(20)	8462(13)
C(37)	10466(20)	4817(28)	9184(17)
C(38)	10054(19)	3866(24)	9576(15)
C(39)	8991(21)	3797(27)	9303(14)
O(40)	6780(5)	4862(8)	8570(4)
C(41)	6345(16)	4195(21)	9205(13)
C(42)	5347(23)	4674(30)	9359(18)
C(43)	5506(15)	6186(20)	9023(12)
C(44)	6348(14)	6126(20)	8452(12)
C(46)	6616(17)	4389(22)	9319(13)
C(47)	5686(14)	4997(20)	9562(12)
C(48)	5218(17)	5632(22)	8936(14)
C(49)	6070(11)	5834(14)	8398(8)

TABLE 3

BOND LENGTHS (Å) AND BOND ANGLES (°) IN 2

Br–Mg	2.622(4)	Mg–C(1)	2.245(11)	Mg–O(12)	2.049(8)
Mg–O(20)	2.146(8)	Mg–O(30)	2.136(9)	Mg–O(40)	2.236(8)
C(1)–C(2)	1.491(15)	C(1)–N(10)	1.482(13)	C(2)–C(3)	1.407(16)
C(2)–C(7)	1.395(16)	C(3)–C(4)	1.380(18)	C(4)–C(5)	1.402(20)
C(5)–C(6)	1.394(20)	C(6)–C(7)	1.424(17)	C(7)–C(8)	1.492(16)
C(8)–C(9)	1.554(16)	C(9)–N(10)	1.515(15)	N(10)–C(11)	1.365(14)
C(11)–O(12)	1.225(14)	C(11)–C(13)	1.547(17)	C(13)–C(14)	1.540(18)
C(13)–C(15)	1.559(20)	C(13)–C(16)	1.541(19)	O(20)–C(21)	1.435(13)
O(20)–C(24)	1.435(14)	C(21)–C(22)	1.562(15)	C(22)–C(23)	1.533(15)
C(23)–C(24)	1.542(16)	O(30)–C(31)	1.427(20)	O(30)–C(34)	1.586(24)
C(31)–C(32)	1.487(29)	C(32)–C(33)	1.662(31)	C(33)–C(34)	1.642(33)
O(30)–C(36)	1.499(22)	O(30)–C(39)	1.327(27)	C(36)–C(37)	1.569(38)
C(37)–C(38)	1.359(39)	C(38)–C(39)	1.565(39)	C(40)–C(41)	1.474(24)
O(40)–C(44)	1.486(22)	C(41)–C(42)	1.509(39)	C(42)–C(43)	1.729(39)
C(43)–C(44)	1.562(30)	O(40)–C(46)	1.455(24)	O(40)–C(49)	1.463(17)
C(46)–C(47)	1.515(31)	C(47)–C(48)	1.466(32)	C(48)–C(49)	1.547(28)
Br–Mg–C(1)	104.3(3)	Br–Mg–O(12)	173.4(3)	Br–Mg–O(20)	94.5(2)
Br–Mg–O(30)	93.9(2)	Br–Mg–O(40)	88.6(2)	C(1)–Mg–O(12)	76.8(3)
C(1)–Mg–O(20)	95.7(4)	Cl–Mg–O(30)	161.8(4)	C(1)–Mg–O(40)	92.4(4)

O(12)–Mg–O(20)	91.9(3)	O(12)–Mg–O(30)	85.2(3)	O(12)–Mg–O(40)	84.9(3)
O(20)–Mg–O(30)	82.1(3)	O(20)–Mg–O(40)	170.4(3)	O(30)–Mg–O(40)	88.6(3)
Mg–C(1)–C(2)	126.1(7)	Mg–C(1)–N(10)	105.2(6)	C(2)–C(1)–N(10)	112.1(8)
C(1)–C(2)–C(3)	118.5(10)	C(1)–C(2)–C(7)	123.4(10)	C(2)–C(3)–C(4)	122.2(11)
C(3)–C(4)–C(5)	119.9(12)	C(4)–C(5)–C(6)	119.4(13)	C(5)–C(6)–C(7)	120.2(12)
C(2)–C(7)–C(6)	120.2(11)	C(2)–C(7)–C(8)	120.2(10)	C(6)–C(7)–C(8)	119.6(10)
C(7)–C(8)–C(9)	111.5(9)	C(8)–C(9)–N(10)	105.0(9)	C(1)–N(10)–C(9)	115.6(8)
C(1)–N(10)–C(11)	117.9(9)	C(9)–N(10)–C(11)	126.1(9)	N(10)–C(11)–O(12)	119.5(10)
N(10)–C(11)–C(13)	120.8(10)	O(12)–C(11)–C(13)	119.7(10)	Mg–O(12)–C(11)	120.6(7)
C(11)–C(13)–C(14)	112.5(10)	C(11)–C(13)–C(15)	112.1(11)	C(11)–C(13)–C(16)	106.3(10)
C(14)–C(13)–C(15)	112.5(11)	C(14)–C(13)–C(16)	105.2(11)	C(15)–C(13)–C(16)	107.5(10)
Mg–O(20)–C(21)	123.2(6)	Mg–O(20)–C(24)	125.4(6)	C(21)–O(20)–C(24)	105.5(8)
O(20)–C(21)–C(22)	105.6(8)	C(21)–C(22)–C(23)	104.9(8)	C(22)–C(23)–C(24)	102.3(9)
O(20)–C(24)–C(23)	105.2(8)	Mg–O(30)–C(31)	121.5(10)	Mg–O(30)–C(34)	122.6(9)
C(31)–O(30)–C(34)	114.3(13)	O(30)–C(31)–C(32)	111.4(16)	C(31)–C(32)–C(33)	105.4(16)
C(32)–C(33)–C(34)	105.7(17)	O(30)–C(34)–C(33)	99.6(15)	Mg–O(30)–C(36)	117.6(10)
Mg–O(30)–C(39)	128.2(13)	C(36)–O(30)–C(39)	112.0(16)	O(30)–C(36)–C(37)	101.6(17)
C(36)–C(37)–C(38)	108.2(23)	C(37)–C(38)–C(39)	105.9(23)	O(30)–C(39)–C(38)	107.9(21)
Mg–O(40)–C(41)	127.8(10)	Mg–O(40)–C(44)	119.9(9)	C(41)–O(40)–C(44)	112.2(13)
O(40)–C(41)–C(42)	111.1(19)	C(41)–C(42)–C(43)	97.5(20)	C(42)–C(43)–C(44)	106.8(18)
O(40)–C(44)–C(43)	104.3(15)	Mg–O(40)–C(46)	125.0(10)	Mg–O(40)–C(49)	125.6(7)
C(46)–O(40)–C(49)	109.4(12)	O(40)–C(46)–C(47)	104.8(17)	C(46)–C(47)–C(48)	110.8(18)
C(47)–C(48)–C(49)	101.6(17)	O(40)–C(49)–C(48)	107.0(13)		

Experimental

X-Ray measurements

Unit cell parameters were determined and intensity data collected on an Enraf–Nonius CAD4 diffractometer using graphite-monochromated Mo-K_α radiation (λ 0.71069 Å).

Crystallization of 2

To a solution of *N*-pivaloyl-tetrahydroisoquinoline (2.0 mmol, 435 mg) in dry THF (5 ml) was added under argon at −78°C t-butyllithium (2.1 mmol; 1.42 ml of a 1.48 *N* solution in pentane). After 1 h magnesium bromide-etherate (2.1 mmol; 0.80 ml of a 2.63 *N* solution in ether) was added, and the solution was allowed to warm up to 0°C and was kept at this temperature for 1 h. The solution was then concentrated to dryness at 0°C in high vacuum, the residue was dissolved in THF (15 ml), pentane (10 ml) was added, and the resulting solution was allowed to stand at −78°C until crystals had formed. After removal of the mother liquor the crystals were dissolved in THF (3 ml) and pentane (3 ml), and the solution was slowly (6°C/6 h) cooled from −10 to −80°C. After removal of the mother liquor, the clear, pale yellow, rhomb-shaped crystals were washed with pentane (2 × 5 ml) and dried in high vacuum at 0°C. A single crystal of suitable size (ca. 0.3 × 0.3 × 0.2 mm) was mounted in a glass capillary tube under argon. Some of the crystals were

TABLE 4

FRACTIONAL ATOMIC COORDINATES ($\times 10^4$) IN *u*-4

Atom	*x*	*y*	*z*
C(1)	4307(3)	1336(2)	7278(3)
C(2)	3510(4)	710(2)	7916(3)
C(3)	2067(4)	776(2)	7974(3)
C(4)	1317(5)	231(3)	8574(4)
C(5)	1981(5)	−397(3)	9110(4)
C(6)	3385(5)	−495(2)	9022(3)
C(7)	4175(4)	51(2)	8420(3)
C(8)	5703(4)	−106(2)	8282(3)
C(9)	6469(4)	643(2)	7915(3)
N(10)	5669(3)	1017(2)	6982(2)
C(11)	6070(4)	1114(2)	5930(3)
O(12)	5312(3)	1491(2)	5259(2)
C(13)	7462(4)	763(2)	5555(3)
C(14)	7513(4)	897(3)	4311(3)
C(15)	8690(4)	1233(3)	6104(4)
C(16)	7599(4)	−150(2)	5754(4)
C(17)	4433(4)	2179(2)	7880(3)
O(18)	4830(3)	2042(1)	9026(2)
C(19)	5562(4)	2690(2)	7390(3)
C(20)	3011(4)	2591(2)	7770(3)
C(21)	2530(4)	2886(2)	6753(3)
C(22)	1201(5)	3216(3)	6620(4)
C(23)	335(5)	3248(3)	7496(4)
C(24)	819(5)	2969(3)	8499(4)
C(25)	2153(4)	2647(2)	8646(3)

TABLE 5

BOND LENGTHS (Å) AND BOND ANGLES (°) IN *u*-4

C(1)–C(2)	1.518(5)	C(1)–N(10)	1.465(4)	C(1)–C(17)	1.575(4)
C(2)–C(3)	1.390(5)	C(2)–C(7)	1.390(5)	C(3)–C(4)	1.380(6)
C(4)–C(5)	1.367(6)	C(5)–C(6)	1.362(6)	C(6)–C(7)	1.402(5)
C(7)–C(8)	1.502(5)	C(8)–C(9)	1.517(5)	C(9)–N(10)	1.472(4)
N(10)–C(11)	1.355(4)	C(11)–O(12)	1.234(4)	C(11)–C(13)	1.541(5)
C(13)–C(14)	1.525(5)	C(13)–C(15)	1.536(5)	C(13)–C(16)	1.534(5)
C(17)–C(18)	1.439(4)	C(17)–C(19)	1.515(5)	C(17)–C(20)	1.522(5)
C(20)–C(21)	1.384(5)	C(20)–C(25)	1.373(3)	C(21)–C(22)	1.387(5)
C(22)–C(23)	1.376(6)	C(23)–C(24)	1.360(6)	C(24)–C(25)	1.388(3)

C(2)–C(1)–N(10)	110.6(3)	C(11)–C(13)–C(15)	109.7(3)
C(1)–C(2)–C(3)	119.6(3)	C(14)–C(13)–C(16)	106.9(3)
C(2)–C(3)–C(4)	121.1(4)	C(1)–C(17)–C(19)	110.7(3)
C(5)–C(6)–C(7)	121.4(4)	O(18)–C(17)–C(20)	110.6(3)
C(6)–C(7)–C(8)	119.8(4)	C(17)–C(20)–C(25)	121.8(3)
C(1)–N(10)–C(9)	113.7(3)	C(21)–C(22)–C(23)	120.5(4)
N(10)–C(11)–O(12)	119.7(3)	C(20)–C(25)–C(24)	120.4(3)
C(11)–C(13)–C(14)	107.6(3)	N(10)–C(1)–C(17)	112.5(3)
C(14)–C(13)–C(15)	107.2(3)	C(3)–C(2)–C(7)	118.5(3)
C(1)–C(17)–O(18)	108.6(3)	C(4)–C(5)–C(6)	119.5(4)
O(18)–C(17)–C(19)	107.6(3)	C(2)–C(7)–C(8)	121.1(3)
C(17)–C(20)–C(21)	119.8(3)	C(8)–C(9)–N(10)	109.1(3)
C(20)–C(21)–C(22)	120.6(4)	C(9)–N(10)–C(11)	127.6(3)
C(23)–C(24)–C(25)	121.3(4)	O(12)–C(11)–C(13)	119.2(3)
C(2)–C(1)–C(17)	113.5(3)	C(11)–C(13)–C(16)	113.2(3)
C(1)–C(2)–C(7)	121.9(3)	C(15)–C(13)–C(16)	111.9(3)
C(3)–C(4)–C(5)	120.3(4)	C(1)–C(17)–C(20)	107.8(3)
C(2)–C(7)–C(6)	119.1(4)	C(19)–C(17)–C(20)	111.5(3)
C(7)–C(8)–C(9)	112.1(3)	C(21)–C(20)–C(25)	118.4(3)
C(1)–N(10)–C(11)	118.6(3)	C(22)–C(23)–C(24)	118.8(4)
N(10)–C(11)–C(13)	121.1(3)		

submitted to an elemental analysis [34]: Found: C, 58.92; H, 7.99; Br, 13.30; Mg, 4.09. $C_{26}H_{42}NO_4BrMg$ calcd.: C, 58.17; H, 7.89; Br, 14.88; Mg, 4.53%.

Crystal data. $(C_{14}H_{18}NOBrMg)\cdot 3THF$, $M = 536.84$, orthorhombic space group $Pna2_1$, a 13.962(6), b 10.614(3), c 17.979(11) Å, at 188 K, $Z = 4$, U 2664.4 Å^3, D_c 1.34 g cm^{-3}. Intensities of 2989 unique reflexions (1418 with $I > 3\sigma(F_0^2)$) were measured for $\theta < 26°$. The structure was solved by the Patterson method using SHELX 84 [35] and refined by full-matrix least squares analysis with anisotropic vibration parameters (isotropic vibration parameters for the THF rings) to $R = 0.0489$, $R_w = 0.0430$ ($w = I/\sigma\ (F_0^2)$) using SHELX 76 [36]. Two of the THF rings were found to be subject to severe disorder. Bond lengths, angles and atomic positions are presented in Tables 2 and 3.

Crystallization of u-4

The compound *u*-4 [9,10] was crystallized from CH_2Cl_2/hexane to give suitable single crystals of which one (approx. size 0.3 × 0.2 × 0.2 mm) was submitted to X-ray crystallographic measurements.

Crystal data. $C_{22}H_{27}NO_2$, $M = 337.47$, monoclinic space group $P2_1/c$, a 9.571(3), b 16.544(6), c 12.102(5) Å, β 92.56(3)°, at 293 K, $Z = 4$, U 1916.3 Å^3, D_c 1.17 g cm^{-3}. Intensities of 4171 unique reflexions ($2009 > 3\sigma$ (F_0^2)) were measured for $\theta < 27°$. The structure was solved by direct methods using MULTAN 80 [37] and refined by full-matrix least squares analysis with anisotropic vibration parameters (non-hydrogen atoms) to $R = 0.0584$, $R_w = 0.0593$ ($w = I/\sigma(R_0^2)$) using SHELX 76 [36]. Bond lengths, angles, and atomic coordinates are presented in Tables 4 and 5. Tables of thermal parameters and structure factors are available from the authors.

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