Crown Ether Grignard Reagents. X-ray Structure of 2-(Bromomagnesio)-1,3-xylyl-15-crown-4

Peter R. Markies,[†] Otto S. Akkerman,[†] Friedrich Bickelhaupt,*[,†] Wilberth J. J. Smeets,[‡] and Anthony L. Spek[‡]

Contribution from the Scheikundig Laboratorium, Vrije Universiteit, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands, and Vakgroep Algemene Chemie, Afdeling Kristal- en Structuurchemie, University of Utrecht, Padualaan 8, 3584 CH Utrecht, The Netherlands.
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Abstract: The first representatives of Grignard reagents with intramolecular crown ether coordination, 2-(bromomagnesio)-1,3-xylyl-15-crown-4 (**1**) and 2-(bromomagnesio)-1,3-xylyl-18-crown-5 (**2**), were obtained by reaction of the corresponding crown ether aryl bromides **3** and **4** in 80 and 16% yield, respectively. During this reaction, a unique and highly specific cleavage of the crown ether ring occurred as an important side reaction. The reaction products were characterized by NMR spectroscopy, by derivatization, and/or by independent synthesis of the derivatization products. The cleavage reaction was shown to require both the presence of the crown ether coordinated Grignard functionality in **1** or **2** and the intermediacy of an extremely reactive, short-lived species, most likely the free carbanion corresponding to **1** and **2**. This postulate gained support from the observation that the same cleavage reaction occurred when bromobenzene was reacted with magnesium in the presence of **1**; in this case, the phenyl anion is proposed as the reactive intermediate. It thus appears that an interesting and hitherto neglected aspect of the famous Grignard formation reaction has become accessible to experimental investigation. In anticipation of novel structural features, the crystal structure of **1** was determined. Crystals of $C_{14}H_{19}O_4MgBr$ (**1**) are monoclinic, space group $P2_1/n$, with unit cell dimensions a = 11.099 (5) Å, b = 14.132 (7) Å, c = 10.113 (6) Å, β = 100.80 (5)°. The crystal structure was solved with direct methods. Anisotropic full-matrix least-squares refinement with 1184 observed reflections and 182 parameters converged at R_F = 0.0691. Remarkable features of the structure are the following: (a) magnesium is hexacoordinated in a strongly distorted pentagonal pyramid with carbon(2) and the four oxygens in the distorted basal plane and bromine at the apex; (b) coordination by oxygens O(2) and O(3) is strong while that of oxygens O(1) and O(4) is weak, which implies that the eight-membered ring chelation is stronger than the five-membered one; (c) external coordination by the solvent tetrahydrofuran does not occur. Surprisingly, the ^{1}H NMR spectrum of **1** in [$^2H_8$]THF revealed equivalence of the benzylic protons (instead of the expected AB pattern); this is explained by rapid dissociation/recombination of the bromide anion.

The coordination between magnesium and ethers or other Lewis bases plays an important role in organomagnesium chemistry.[1] Recently, Richey and co-workers have demonstrated that polycoordination of dialkylmagnesiums by cryptands and crown ethers can have a spectacular influence on the structure and reactivity of these reagents.[2] Intramolecular coordination of organomagnesium compounds has received less attention so far, although dramatic effects have been encountered in a number of cases, too.[3-5]

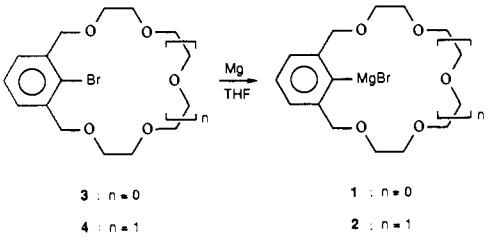
As we are engaged in a broad investigation of intramolecular coordination in Grignard reagents,[4-6] it seemed promising to combine the features of intramolecular and polycoordination. We here report some unexpected results encountered during the synthesis and structural investigation of the crown ether Grignard reagents 2-(bromomagnesio)-1,3-xylyl-15-crown-4 (**1**) and 2-(bromomagnesio)-1,3-xylyl-18-crown-5 (**2**). The corresponding lithium compounds have very recently been reported by Reinhoudt and co-workers.[7]

Results and Discussion

Synthesis and Byproducts. The synthesis of **1** and **2** was attempted in the normal fashion by reacting the corresponding aryl bromides **3** and **4**, respectively, with magnesium metal. In diethyl ether as solvent, **4** was quantitatively recovered after stirring for 5 days at room temperature. In THF, a ready reaction took place. To our surprise, and contrary to our experience with most acyclic analogues of **1** and **2**,[6c] the yields of **1** (80%) and particularly of **2** (16%) were lower than normal, even when the reactions were performed under ideal circumstances, i.e., with triply sublimed magnesium and highly purified reagents in an evacuated, fully sealed glass apparatus (Scheme I; cf. Experimental Section).

Hydrolysis of the reaction mixture and titration of the aqueous phase with HCl and EDTA revealed that the starting bromides **3** and **4** had been completely consumed to produce "basic" and

Scheme I



"total" magnesium ions as if the sequence of eq 1 had occurred quantitatively under formation of magnesium bromide hydroxide.

$$\underset{\mathbf{3, 4}}{ArBr} + Mg \rightarrow \underset{\mathbf{1, 2}}{ArMgBr} + H_2O \rightarrow \underset{\mathbf{5a, 6a}}{ArH} + HOMgBr \quad (1)$$

The analogous deuteriolysis, followed by GCMS analysis, confirmed the absence of **3** or **4**, but the expected deuteriolysis products ArD, **5b** or **6b**, respectively, were strongly contaminated by their protonated analogues **5a** or **6a**. This implies that **5a** or **6a** was already present in the reaction mixture before deuteriolysis

[†] Vrije Universiteit.
[‡] University of Utrecht.

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(2) (a) Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672. (b) Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 432. (c) Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *Organometallics* **1985**, *4*, 1154. (d) Richey, H. G., Jr.; Kushlan, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 2510.
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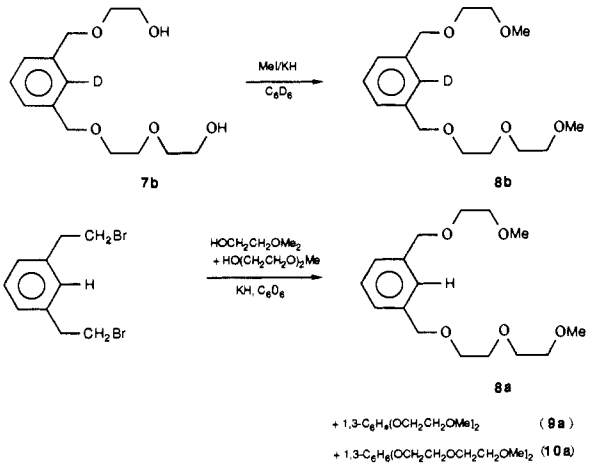
Scheme II



and consequently that the correct magnesium analysis corresponding to eq 1 was straightforward only at first sight.

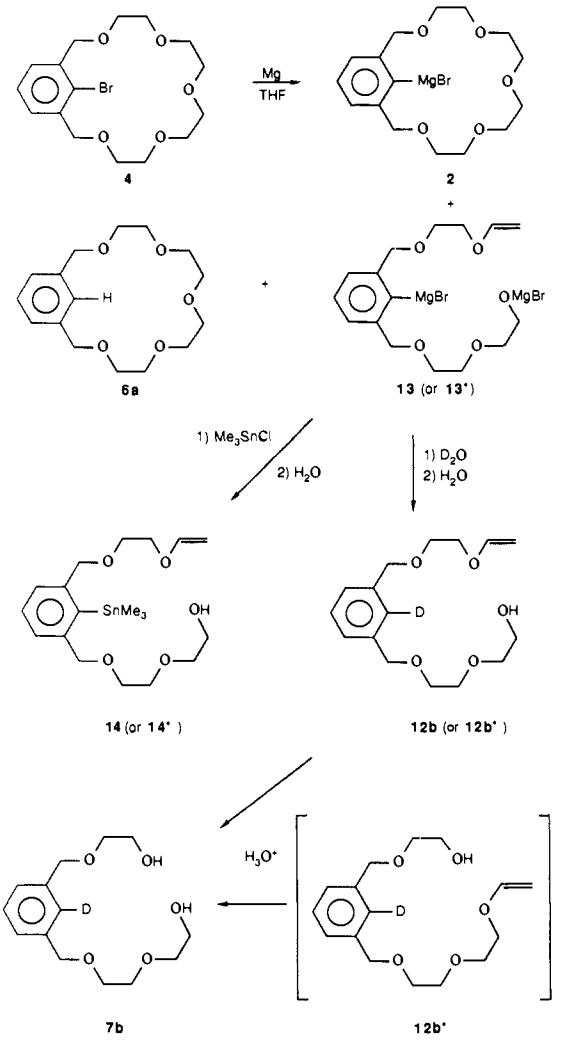
The deuteriolysis products in the "crown-5" series were subjected to column chromatography which separated **6a** + **6b** from one unexpected, highly polar product. As discussed later on, a highly specific cleavage of the crown ether ring had occurred yielding diol **7b** (Scheme II) whose identity was established as follows. Treatment with methyl iodide and potassium hydride in benzene converted **7b** to its dimethyl ether **8b** which was characterized by its NMR and mass spectra. The reference compound **8a** was independently prepared together with the lower and higher homologues **9a** and **10a**, respectively, by reaction of 1,3-bis(bromomethyl)benzene with a 1:1 mixture of methyl cellosolve and methyl carbitol (Scheme II); the GCMS data of **8a** were identical with those of **8b** from the Grignard reaction with the remarkable exception that the latter turned out to be fully deuteriated at the aromatic 2-position. This proves that **7b** was formed from a precursor present in the Grignard formation mixture which was still carrying an organomagnesium function at the 2-position before deuteriolysis. The quantitative analysis of products from **4** revealed the following yields: **6a** 44%, **6b** 16%, **7b** 40%.

Independent evidence for the structure and genesis of **6a**, **6b**, and **7b** was derived from the following experiments. The origin of the hydrogen at C-2 in **6a** was traced by performing the reaction between **4** and magnesium in [$^2H_8$]THF, followed by hydrolysis with H_2O; GCMS analysis showed that only **6a**, and no **6b**, was present. It was thus established that the hydrogen in question is not abstracted from the solvent, but from one of the products derived from **4**. The identity of the Grignard reagent **2** as the precursor of **6b**, and its yield, were corroborated by derivatization with chlorotrimethylstannane which gave 2-(trimethylstannyl)-1,3-xylyl-15-crown-5 (**9**) in 17% yield (eq 2). Interestingly, this derivatization reaction did not occur at 25 °C; **2** remained unchanged and, on addition of water, was hydrolysed to give **6a**. This may be taken as an indication of steric hindrance in **2**. Only at 50 °C does the reaction proceeded in a practically quantitative fashion, as evidenced by the yield of **11** (17%) being close to that of **6b** in the deuteriolysis reaction (16%).

$$\underset{\mathbf{2}}{\mathrm{ArMgBr}} + \mathrm{ClSnMe_3} \xrightarrow{50\ ^\circ\mathrm{C}} \underset{\mathbf{11}}{\mathrm{ArSnMe_3}} \qquad (2)$$

The direct precursor of **7b** was discovered when the workup of the reaction mixture after deuteriation was performed with special care, avoiding acidic conditions. In this case, instead of **7b**, a monovinyl ether thereof was obtained which on acid hydrolysis was converted to **7b**. This vinyl ether **12b** (Scheme III) was probably a single product; it could so far not be established at which of the two hydroxyl groups of **7b** the vinyl ether function is attached, as both **12b** and **12b′** will yield **7b** on hydrolysis. In any case, this result allows the conclusion that the primary ether cleavage product in the Grignard reaction mixture was **13** (or its regioisomer **13′**, cf. **12b′** and Scheme VIII) which carries a carbon-bonded magnesium function at position 2 (Scheme III). The

Scheme III

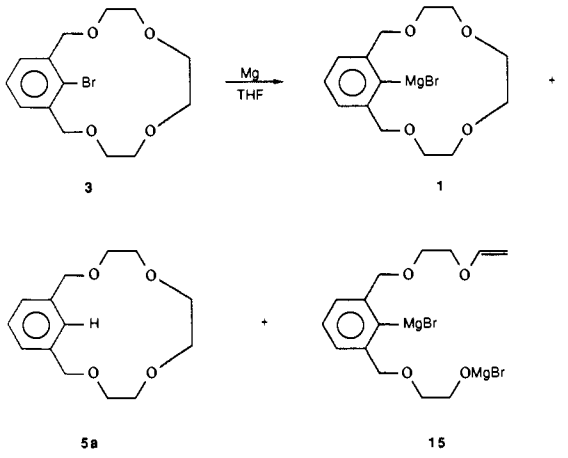


identity of **13** was further supported in a tentative way by a side product obtained in the reaction of the crude Grignard reaction mixture with chlorotrimethylstannane (cf. eq 2). In the 25 °C version of this reaction, when **2** remained unchanged, **13** was readily derivatized to give **14** (or **14′**; Scheme III); clearly, the steric hindrance impeding the normal reaction of **2** is not present, and not expected to be so, in **13**. Because of its sensitive vinyl ether function, **14** could not be isolated in pure form. However, the reaction mixture contained **14** and **6a** only, so that certain features of the structure of **14** could be derived from the ^1H NMR spectrum of the mixture; in particular, the Me_3Sn group and part of the characteristic ABX system of the vinyloxy group were identified (see Experimental Section), while other signals coincided with those of **6a**. In the 50 °C version of this experiment, the ratio of **6a**:**11**:**14** (corresponding to **6a**:**2**:**13**) was 46:17:39, in excellent agreement with the results obtained in the D_2O quench (vide supra).

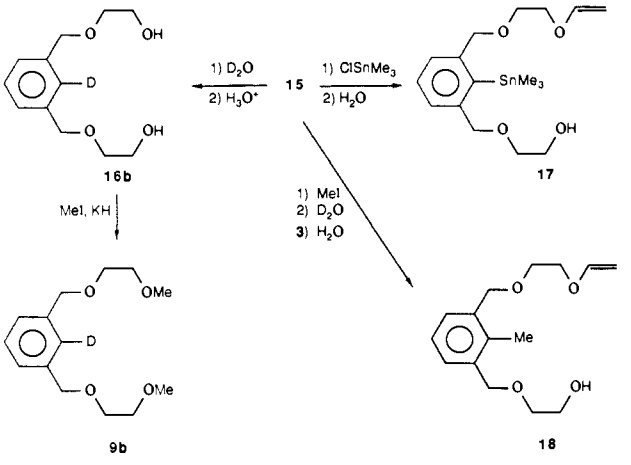
Another important observation was that the original Grignard reaction mixture was stable. When it was stored in a fully sealed glass apparatus, so that air and moisture were absolutely excluded, and then deuteriolyzed after several months, the product distribution was essentially unchanged (see Experimental Section). This means that the formation of **6a** and **13** occurs only during the process of Grignard formation. We shall return to this interesting point in the final section.

In the "crown-4" series, the course of the reaction and the products were qualitatively analogous and supported the conclusions reached for the "crown-5" series. An important and pleasant difference was, however, the much higher yield of the Grignard reagent **1** (80%). Contrary to **2**, **1** was only very slightly soluble in THF and precipitated during the reaction; we shall

Scheme IV



Scheme V



discuss in the final section that the low solubility and the high yield of **1** are closely interrelated.

It is of interest to point out that in contrast to **2**, **1** did not at all react with chlorotrimethylstannane, not even at 50 °C. This behavior is rather unusual for a Grignard reagent; it probably signals that **1** is an extremely crowded molecule which cannot easily be attacked by a bulky reagent such as chlorotrimethylstannane.

By cooling the crude Grignard reaction mixture, **1** was nearly completely removed by precipitation and the mother liquor was decanted for easier investigation of the side products **5a** (10%) and **15** (10%) (Scheme IV). Compound **5a** corresponds to **6a**; both are present as such in the reaction mixture before hydrolysis of deuteriolysis. On deuteriolysis of the total reaction mixture, **1** gave **5b** (80%), while **5a** (10%) remained unchanged. Compound **15** is the counterpart of **13** (Scheme III); **15** was characterized by three derivatization sequences of the decanted mother liquor (vide supra; Scheme V). In analogy to the sequence **13** → **7b** → **8b**, **15** was deuteriolyzed and the resulting diol **16b** was converted to the dimethyl ether **9b** with potassium hydride/methyl iodide in benzene; **9b**, like **8b**, was fully deuteriated at the 2-position (GCMS, ^{1}H NMR). The vinyl ether function could be conserved in the reaction of **15** with chlorotrimethylstannane followed by careful hydrolysis under acid free conditions to furnish **17**. In the third derivatization reaction, **15** gave, with an excess of methyl iodide (room temperature, 4 days), **18** (in a 1:1 mixture with **5a**). The latter was characterized by its ^{1}H NMR spectrum which showed the presence of the arylmethyl group (δ 2.33) and of the vinyloxy group (ABX system; see Experimental Section).

The Structure of 1. The high yield and low solubility of **1** facilitated the isolation of crystals which were suitable for X-ray crystal structure determination. These crystals were obtained by slow crystallization of **1** by evaporation of a saturated solution in THF (3.4 mmol/L). The monoclinic unit cell contains four discrete molecules of **1** (Figure 1). Bond distances, bond angles,

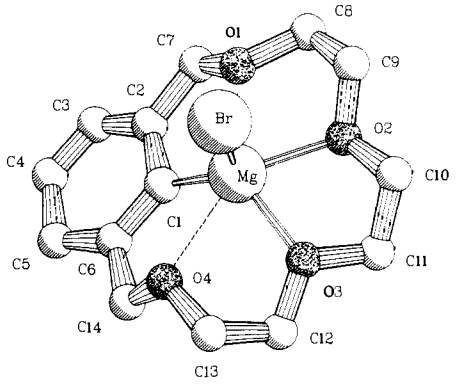


Figure 1. PLUTO drawing (EUCLID version) of **1** with the adopted atom numbering. Hydrogen atoms are omitted for clarity.

Table I. Bond Distances (Å), Bond Angles (deg), and Selected Torsion Angles (deg) for the Non-Hydrogen Atoms of **1**

Br-Mg	2.517 (4)	C(1)-C(2)	1.43 (2)
Mg-O(2)	2.13 (1)	C(1)-C(6)	1.38 (2)
Mg-O(3)	2.12 (1)	C(2)-C(3)	1.33 (2)
Mg-C(1)	2.10 (1)	C(2)-C(7)	1.44 (3)
O(1)-C(7)	1.44 (2)	C(3)-C(4)	1.29 (4)
O(1)-C(8)	1.46 (2)	C(4)-C(5)	1.43 (3)
O(2)-C(9)	1.38 (2)	C(5)-C(6)	1.44 (2)
O(2)-C(10)	1.42 (2)	C(6)-C(14)	1.48 (3)
O(3)-C(11)	1.42 (2)	C(8)-C(9)	1.44 (3)
O(3)-C(12)	1.42 (2)	C(10)-C(11)	1.51 (3)
O(4)-C(13)	1.43 (3)	C(12)-C(13)	1.45 (3)
O(4)-C(14)	1.42 (2)		

Br-Mg-O(2)	97.4 (3)	C(1)-C(2)-C(3)	121 (2)
Br-Mg-O(3)	98.8 (3)	C(1)-C(2)-C(7)	121 (1)
Br-Mg-C(1)	128.2 (4)	C(3)-C(2)-C(7)	118 (2)
O(2)-Mg-O(3)	73.9 (4)	C(2)-C(3)-C(4)	122 (2)
O(2)-Mg-C(1)	124.4 (4)	C(3)-C(4)-C(5)	124 (2)
O(3)-Mg-C(1)	119.7 (4)	C(4)-C(5)-C(6)	113 (2)
C(7)-O(1)-C(8)	116 (1)	C(1)-C(6)-C(5)	122 (2)
Mg-O(2)-C(9)	114.3 (9)	C(1)-C(6)-C(14)	117 (1)
Mg-O(2)-C(10)	113 (1)	C(5)-C(6)-C(14)	121 (2)
C(9)-O(2)-C(10)	113 (1)	O(1)-C(7)-C(2)	109 (1)
Mg-O(3)-C(11)	116 (1)	O(1)-C(8)-C(9)	108 (1)
Mg-O(3)-C(12)	121.7 (9)	O(2)-C(9)-C(8)	108 (2)
C(11)-O(3)-C(12)	114 (1)	O(2)-C(10)-C(11)	104 (2)
C(13)-O(4)-C(14)	117 (1)	O(3)-C(11)-C(10)	106 (1)
Mg-C(1)-C(2)	117.4 (8)	O(3)-C(12)-C(13)	108 (1)
Mg-C(1)-C(6)	124.4 (9)	O(4)-C(14)-C(6)	110 (1)
C(2)-C(1)-C(6)	117 (1)	O(4)-C(13)-C(12)	111 (2)

C(8)-O(1)-C(7)-C(2)	152 (1)	C(13)-O(4)-C(14)-C(6)	-151 (1)
C(7)-O(1)-C(8)-C(9)	-155 (1)	C(1)-C(2)-C(7)-O(1)	-19 (2)
C(10)-O(2)-C(9)-C(8)	169 (1)	C(1)-C(6)-C(14)-O(4)	27 (2)
C(9)-O(2)-C(10)-C(11)	-178 (1)	O(1)-C(8)-C(9)-O(2)	47 (2)
C(12)-O(3)-C(11)-C(10)	-174 (2)	O(2)-C(10)-C(11)-O(3)	-54 (2)
C(11)-O(3)-C(12)-C(13)	168 (2)	O(3)-C(12)-C(13)-O(4)	53 (2)
C(14)-O(4)-C(13)-C(12)	88 (2)		

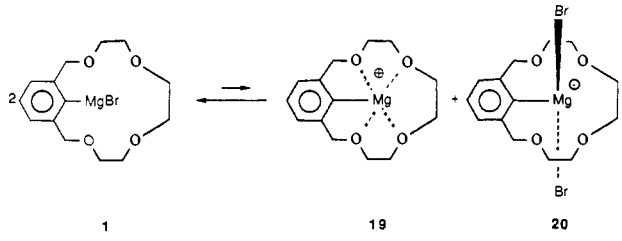
and relevant torsion angles are presented in Table I. A thermal motion ellipsoid plot indicates high rigid body rotational motion of the molecule approximately about the Mg-Br bond (see Supplementary Material). The molecules are weakly linked via C-H···Br hydrogen-bond-type short contacts [H(71)···Br = 2.89 (2) Å; ∠C(7)—H(71)···Br = 166 (2)°].

Compound **1** is the first example of a Grignard reagent engaged in an intramolecular crown ether coordination. At first sight, the structure appears to be that of a rather normal Grignard reagent with magnesium being surrounded by C(1) (d = 2.10 (1) Å), Br (d = 2.517 (4) Å), O(2) (d = 2.13 (1) Å), and O(3) (d = 2.12 (1) Å) in the center of a distorted tetrahedron. The bond lengths and angles are close to those of other Grignard reagents,[1] although it may be significant that the Mg-C bond is slightly shorter than normal, while the bonds to O and Br are slightly longer. On closer inspection, a number of remarkable features can be discerned.

(1) The oxygens O(1) (d = 2.33 (1) Å) and O(4) (d = 2.49 (1) Å) are farther removed from Mg than those of normal Grignard reagents,[1] but both their distance and their orientation suggest a weak coordination.

(2) If one takes the total coordination sphere into account, it can be described as a pentagonal pyramid with bromine in the

Scheme VI



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apex; the basal plane is formed by the four oxygen atoms, which are coplanar within 0.06 Å, and C(1), which is 1.06 (2) Å below the plane of the oxygens. The distance of the magnesium atom is 0.48 (1) Å from the pentagonal plane and 0.27 (1) Å from the plane of the four oxygens.

(3) In this situation, magnesium is electronically sufficiently saturated so that the coordination of an additional molecule of THF is not required, even though THF is a strongly basic ether toward magnesium. Coordination of THF would be difficult for steric reasons, too.

(4) It is somewhat unexpected that the coordination to O(2) and O(3) (eight-membered chelates!) is stronger than that to O(1) and O(4) (five-membered chelates!). As long as further material for comparison is lacking, it cannot be decided whether this is due to conformational restraints of the metacyclophane skeleton of the crown ether ligand or to an inherent thermodynamic preference of the eight-membered chelate over the normally more favorable five-membered chelate. The latter possibility deserves further investigation, as in our case, the five-membered-ring system is probably rather strained due to the long bonds to magnesium. Preliminary thermochemical results support this interpretation.[6c]

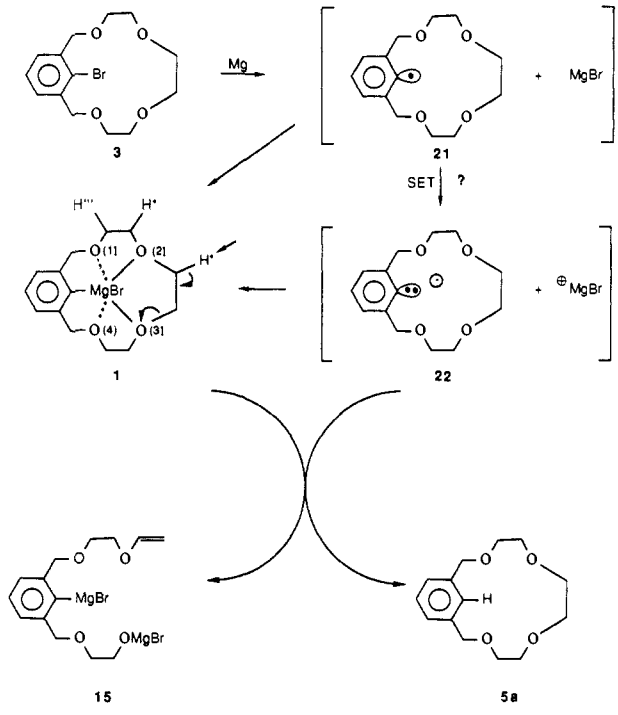
(5) The spatial orientation of the four oxygens toward magnesium is somewhat variable: the angle between Mg–O and the bisector of the C–O–C angle is 39°, 43°, 27°, and 50° for O(1), O(2), O(3), and O(4), respectively. All these values are closer to 50–60°, the value expected for coordination via the oxygen lone pairs, than to O°, which would be indicative of a purely dipolar coordination with an orientation between the two lone pairs.

The structure of **1** probably persists also in solution. For the reasons indicated under point 3, it is unlikely that THF participates in the solvation of the magnesium. Unfortunately, the low solubility made a determination of the degree of association impossible, but there is no reason to doubt that **1** occurs as a monomeric species, as this is typical for simple Grignard reagents in THF[1]; the congestion present in **1** forms an additional bias against dimerization.

The ^{1}H NMR spectrum of **1** in [$^2H_8$]THF was remarkably simple. The most surprising feature was the singlet of the benzylic methylene groups (δ 4.66), because in the "crown-4" series, most compounds bearing a substituent at the 2-position have an AB quartet for the benzylic methylene protons; besides **1**, only **5** shows a singlet. For example, **3** shows an AB spectrum, presumably because the metacyclophane bridge can flip around the benzene ring neither at the front, where it is hindered by the bulky bromine substituent, nor at the back side of the benzene ring. It is therefore extremely unlikely that flipping of the bridge is the mechanism which brings about equivalence of the benzylic methylene protons in **1**. We also consider it rather unlikely that in **1** the methylene protons are accidentally isochronous, or that equivalence is achieved via a Schlenk equilibrium which would involve the exceedingly crowded Ar_2Mg. A rather tempting speculation is that the bromide ion dissociates from the magnesium. As mentioned above, the Mg–Br distance of 2.517 (4) Å is only slightly longer than in model compounds, so that the crystal structure does not provide strong arguments for predissociation. On the other hand, the situation in solution may be different, and a small degree of dissociation, if sufficiently rapid, could explain the coalescence of the benzylic proton signals by the mechanism shown in Scheme VI.

Dissociation of **1** gives cation **19** in which a minimal movement of the magnesium toward the basal pentagonal plane creates a

Scheme VII



species with a mirror plane through the benzene ring, to which the bromide ion could return from either side. If this process is fast on the NMR time scale, it makes the two sides of the benzene ring, and thus the benzylic protons, equivalent. A precedent for such a dissociation may be found in the work of Richey,[2b,d] where a dialkylmagnesium has been shown to dissociate into an alkylmagnesium cation and an alkyl anion. One would expect such a dissociation process to be easier in the case of the much more stable bromide ion, but in analogy to Richey's case, assistence by a second molecule of **1**, which complexes the anion and forms a magnesiate complex such as **20**, seems a likely course of events.

The Mechanism of Grignard Formation. The crystal and molecular structure of **1**, besides being interesting because of the unusual coordination of magnesium, also gave valuable information which helped to better understand the peculiar abnormalities observed in connection with the formation reaction of **1** and **2**. A rather consistent and detailed picture can be drawn, although, as we will show, one challenging uncertainty remains. Our proposal is illustrated for the case of **1** (Scheme VII). The most remarkable feature is the unusual prominence of ether cleavage product **15** (or of **13**, respectively, in the case of **2**), and it will be explained by postulating attack of a not yet fully identified short-lived intermediate on the Grignard reagent **1** (or **2**, respectively).

It is generally agreed that the Grignard formation reaction proceeds by reaction of the organic halide and magnesium via an intermediate organic radical (and magnesium subhalide), e.g., **3** → **21**. Normally, rapid combination leads to the Grignard reagent (i.e., **1**); intermediate stages in this latter process have not been identified and are normally not discussed explicitely (vide infra).[1,8]

It is important to emphasize that the cleavage reaction does not involve an intramolecular (radical) reaction such as hydrogen abstraction within **21**, as this would lead to a cleavage product with a hydrogen at the aromatic 2-position; in fact, both cleavage products (**15** and **13**) fully retain the organomagnesium function at this position.

In the special case of **1**, the reaction seems to derail to some extent because one of the intermediates attacks **1** already present.

(8) (a) Walborsky, H. M.; Banks, R. B. *Bull. Soc. Chim. Belg.* **1980**, *84*, 849 and reference cited therein. (b) Schaart, B. J.; Blomberg, C.; Akkerman, O. S.; Bickelhaupt, F. *Can. J. Chem.* **1980**, *58*, 932 and references cited therein. (c) Garst, J. F.; Deutsch, J. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1986**, *108*, 2490.

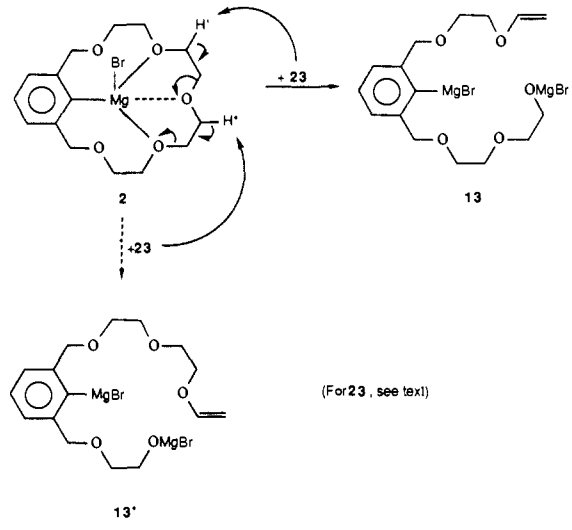
Apparently, **1** is, more than normal Grignard reagents, activated by the coordination between magnesium and the oxygen atoms. The crystal structure tells us that it is O(2) and O(3) which are most strongly bound, and this explains why the attack of the cleaving reagent starts with high specificity at these and not at other oxygen atoms; intuitively, one might have guessed that the benzylic oxygens would be more vulnerable.[9] About the identity of the cleaving reagent, one can only speculate at the moment. Both the radical species **21** and the carbanionic species **22**, formed from **21** by single electron transfer (SET), are, in principle, candidates.

There is ample evidence in the literature for the intermediacy of radicals (analogous to **21**) in the formation of Grignard reagents.[1,8] The corresponding carbanions (analogous to **22**) have received much less attention and little is known about their possible involvement, presumably because they are much more reactive and have an even lower steady state concentration than the radicals. There is, in fact, a claim that carbanions do normally occur as intermediates,[10] but in the light of current insight, the arguments presented do not appear to be compelling. Perhaps somewhat more convincing, carbanions have been postulated to explain the formation of hydrocarbon byproducts from optically active cyclopropyl halides with (some) retention of configuration, because the cyclopropyl radical is known to racemize completely.[11] More conclusive evidence on intermediate carbanions or comparable species is available for the reaction of alkyl halides with alkali metals or aromatic radical anions.[12]

We feel that the cleavage reactions occurring in the formation of **1** and **2** may form unique and particularly sensitive indicators for the occurrence of these fleeting and evasive carbanionic intermediates in the Grignard formation reaction. We prefer to explain the cleavage by the involvement of **22** over that of **21**, because it is difficult to understand why a highly regiospecific radical attack at the ether bridge should be promoted by metal coordination, whereas activation of an α-CH bond, which is polarized by coordination of magnesium to the neighboring oxygen O(2), toward attack by the very reactive, more or less free carbanion **22** offers a reasonable explanation. A certain analogy may be found in the behavior of organolithiums, which have a rather pronounced carbanionic character, toward ethyleneglycol ethers.[7,13] Furthermore, coordination of magnesium to the neighboring O(3) in **1** makes O(3) a better leaving group in a concerted, E2-type process as indicated by the arrows in Scheme VII. Probably for this reason, the attack of **22** on **1** takes place preferentially at H′ and not at H″. One can exclude the possibility that the elimination reaction is governed by differences in antiperiplanar orientation of the H–C–C–O groupings involved, as the torsion angles are equally favorable for all the possible E2-combinations. It should also be emphasized that the combination of H‴ with O(2) is less favorable because H‴ is less activated by the weakly coordinated O(1) than H′ is by O(2).

By a similar line of reasoning, one can explain the highly specific cleavage of **2** to **13** (Scheme VIII). Assuming that **2**, like **1**, has the strongest coordination between magnesium and O(2) (or O(4); both involve eight-membered chelates!), H′ would be the activated

Scheme VIII



proton which is abstracted by the "reactive intermediate" **23** (a carbanion analogous to **22**) as indicated by the arrows in Scheme VIII; this furnishes **13**. An alternative, preferential coordination of magnesium to O(3) would elicit attack of **23** at H″ which leads to **13′**. In any case, strong coordination at and activation of CH bonds α to the benzylic O(1) or O(5) is excluded by the structure of the final cleavage product **7b** (Scheme III). Unfortunately, the unknown regiochemistry of **12b** and the lack of crystals of **2** suitable for X-ray structure determination have so far prevented an answer to the question of coordination and probable point of cleavage in **2**.

In this context, it should be mentioned that Richey and coworkers[2c] observed a similarly specific cleavage reaction of the [2.1.1]cryptand in its complex with dineopentylmagnesium. In their case, orientational effects (i.e., torsion angles) and leaving group preferences (O > N) apparently determine the cleavage site.

The proposed mechanism also nicely explains other unique aspects of the side reaction. Proton abstraction from **1** by **22** leads to **15** and **5a** (Scheme VII), respectively; stoichiometry requires that these products are formed in a 1:1 ratio as was actually observed for **1** (and, ceteris paribus, for **2**). The outcome of the magnesium titrations (cf. eq 1) is also accounted for: 2 mol of base and 2 mol of magnesium ions are found, though not exclusively from 2 mol of **1** as believed initially; rather, for the major part, 2 mol of **1** are replaced by 1 mol of **15** giving the same titration results, while the corresponding **5a** makes no contribution to the magnesium titrations. Furthermore, in line with experimental results, the mechanism predicts that the organomagnesium functionality is retained in the cleavage product **15**, while the intact crown ether product **5a** has lost the magnesium function due to protons which are ultimately derived from the ether part of the substrate **3**, but not from the solvent THF. The same line of reasoning applies to the reactions involving **4**.

Finally, the difference in yield between **1** and **2** can be rationalized. If, as postulated by our mechanism, the cleavage reaction does only occur on the Grignard reagent already formed, then its availability will determine the degree of cleavage. In the case of **1**, the Grignard is removed from the reaction medium due to its low solubility and is thus protected from attack by **22**. In contrast, the soluble **2** builds up a higher concentration which favors the bimolecular cleavage process; this is particularly important as the steady state concentration of the other partner in the cleavage reaction, i.e., **23**, is extremely low.

An independent check for the correctness of some of these assumptions was obtained by the use of bromobenzene instead of **3** or **4** as a source of the postulated "reactive intermediates" **22** or **23**. First, we checked that phenylmagnesium bromide and **1** gave no reaction within 1 week at room temperature. Then, a tenfold molar excess of phenylmagnesium bromide was prepared

(9) See for instance the cleavage of benzylic ethers with activated magnesium (Bartmann, E. *J. Organomet. Chem.* **1987**, *332*, 19. Maercker, A. *Angew. Chem.* **1987**, *99*, 1002) or under the conditions of mass spectroscopy ((16), vide infra)).

(10) Andrac, M.; Gaudemar, F.; Gaudemar, M.; Gross, B.; Miginiac, L.; Miginiac, P.; Prêvost, C. *Bull. Soc. Chim. Fr.* **1963**, *1385*, and references cited therein.

(11) Walborsky, H. M.; Aronoff, M. J. *J. Organomet. Chem.* **1973**, *51*, 55.

(12) Garst, J. F. *Acc. Chem. Res.* **1971**, *4*, 400.

(13) (a) Ellison, R. A.; Kotsonis, F. N. *J. Org. Chem.* **1973**, *38*, 4192. (b) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1984**, *49*, 209.

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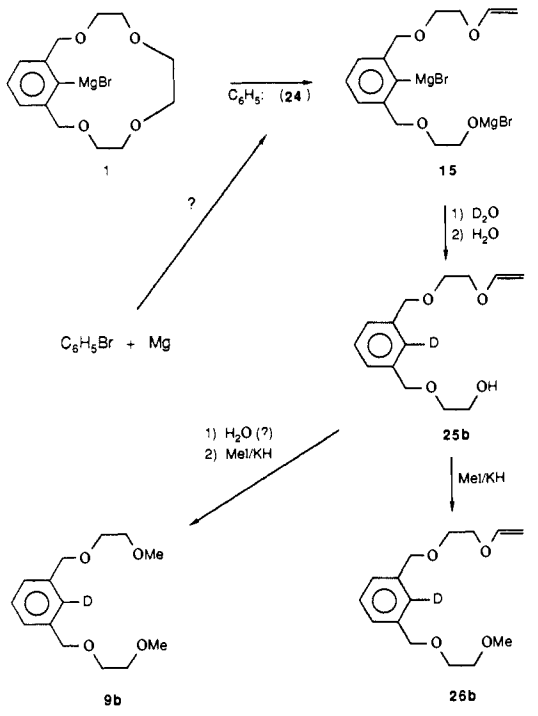
(15) Vreugdenhil, A. D.; Blomberg, C. *Recl. Trav. Chim. Pays-Bas* **1963**, *453*, 461.

(16) Gray, R. T.; Reinhoudt, D. N.; Smit, C. J.; Veenstra, I. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 258.

(17) Gray, R. T.; Reinhoudt, D. N.; Spaargaren, K.; de Bruijn, J. F. *J. Chem. Soc., Perkin Trans. II* **1977**, 206.

Scheme IX



in THF from bromobenzene and magnesium in the presence of **6a**; **6a** was recovered quantitatively, and cleavage products such as **7a** could not be detected by ^1H NMR spectroscopy. However, when a tenfold molar excess of bromobenzene and magnesium was reacted in the presence of **1** under the same reaction conditions, followed by quenching with D_2O (and finally aqueous workup), **1** was completely converted to a new product **25b** (Scheme IX); **5a** and **5b** were not detectable. The cleavage product **25b** is the analogue of **12b** (Scheme III). It was characterized by its ^1H NMR spectrum and by conversion to its methyl ether **26b**; both compounds were fully deuteriated at the aromatic 2-position. As **25b** is rather sensitive toward hydrolysis, the vinyloxy group was probably inadvertently cleaved off to a small extent during the process of converting **25b** to **26b**; the resulting diol **16b** was apparently methylated together with the bulk of **25b** and gave the dimethyl ether **9b** as a byproduct (cf. also Scheme V). Both the conversion of **25b** to **9b** and the retention of the vinyloxy group in **26b** may, incidentally, be considered as supportive evidence for the structure assignment to the primary cleavage product **15**.

We assume that during the formation of phenylmagnesium bromide, a reactive intermediate **24**, analogous to **22** (Scheme VII) and **23** (Scheme VIII), is present in the solution; if our working hypothesis is correct, it should in this case be the phenyl anion. It behaves like the other intermediates and cleaves **1** under formation of **15**, again under full conservation of the organomagnesium function in the cleavage product. As pointed out before, in view of the presumbably very low steady state concentration of **24** (and of the other postulated carbanions), the high efficiency of the cleavage reactions is surprising.

Conclusions

Two interesting and novel aspects have been encountered in the investigation of the novel crown ether Grignard reagents **1** and **2**. In the first place, the crystal structure of **1** revealed an unprecedented mode of coordination for a Grignard reagent: a distorted pentagonal pyramid. Second, the byproducts **5a** and **6a**, but especially the ether cleavage products **13** and **15**, are not only unusual as such, but may help in tracing more sophisticated aspects of the Grignard formation reaction, a reaction that is of great theoretical and practical interest. At present, the proposed carbanionic intermediate seems to explain most of the experimental observations in a satisfactory way, but it does need further corroboration.

Experimental Section

The NMR spectra we measured on a Bruker WH 90 (^1H, 90 MHz) or a Bruker WH 250 (^1H, 250 MHz, or ^{13}C, 62.89 MHz) in $CDCl_3$ unless otherwise stated. The 400 MHz spectrum of **8a** was measured on a Bruker MSL 400. Some of the experiments were performed with use of a high vacuum dried, sealed glass apparatus. GCMS analyses was performed on a HP 5890 GC/5970 MS combination, operating at 70 eV and equipped with a Chrompack CP Sil 19CB 51 m/0.21 mm column.

Dry THF was prepared by distillation from $LiAlH_4$ after predrying on KOH, or, in sealed glassware, by distillation from liquid Na-K alloy. The starting materials potassium hydride (Janssen, 40% in liquid paraffin), methyl iodide, chlorotrimethylstannane, 1,3-bis(bromomethyl)-benzene (Janssen), and 1-bromo-2,6-dimethylbenzene (Janssen) were commercially available. Triethyleneglycol (Baker grade) and tetraethyleneglycol (Merck) were dried on molecular sieve 4Å. Column chromatography was performed with Al_2O_3 (Merck, activity II–III). For all Grignard preparations, we used triply sublimed magnesium (0.5–1 cm, unless otherwise stated). For the determination of yields, samples of Grignard reagents were hydrolized and the aqueous phase titrated with HCl for "basic" Mg^{2+} and EDTA for "total" Mg (cf. eq 1).

Syntheses of Starting Materials. 1-Bromo-2,6-bis(bromomethyl)-benzene was prepared by direct photolytic bromination of 1-bromo-2,6-dimethylbenzene.[6c] The crown ethers **3**[7], **4**[7], and **6a** are known in literature; they were synthesized from the appropiate oligoethyleneglycol and 1,3-bis(bromomethyl)benzene in the presence of KH.

Reaction of 4 with Magnesium in THF. In a high-vacuum sealed glass apparatus, **4** (1.5 g, 4.0 mmol) was stirred with magnesium (1.0 g, 42 mmol, finely divided) in dry THF (100 mL). After 1 week of stirring, the black magnesium dust was allowed to settle. The clear solution was decanted into a second vessel connected to the reaction vessel. Titration of a sample showed that 3.85 mmol of base and 3.62 mmol of Mg^{2+} were present (90–95%); the close to 1:1 ratio would correspond to the presence of ArMgBr (see, however, the discussion around eq 1). The solution was quenched with D_2O and evaporated to dryness. After addition of 200 mL of diluted aqueous HCl, the organic material was isolated by extraction with CH_2Cl_2. The CH_2Cl_2 phase was dried on $MgSO_4$ and filtered, and the solvent was evaporated, yielding 2.10 g of a yellowish oil as residue. The ^1H NMR spectrum (90 MHz) indicated that at least three products are present, including **6a** and **6b**.

In another experiment 5 mmol of **4** was reacted, and the magnesium used was not finely divided. Titration showed that 5.17 mmol of total base and 5.05 mmol of Mg^{2+} are present, so the conversion appears to have been practically quantitative. The ^1H NMR (90 MHz) spectrum showed the same product mixture to be present. The crude oils from both reactions were combined and subjected to column chromatography (Al_2O_3 column 1 × 25 cm, petroleum ether 40–60 °C/THF mixtures as eluent, starting at 10% THF; fractions of 100 mL were collected, the concentration of THF being raised each time with 10%). The first three fractions (10–30% THF) contained a mixture of **6a** and **6b**, which solidified to give colorless crystals; yield 1.31 g (4.4 mmol); 26% deuterium incorporation according to the GCMS mass spectrum. From 40 to 80% THF, followed by 100 mL of 5% H_2O in THF 0.80 g of a yellowish oil was eluted, which contained 3.0 mmol of **7b** as the only component, according to the ^1H NMR (250 MHz) spectrum. The ratio of **6a**:**6b**:**7b** was 44:16:40.

[2-^{2}H]-1,3-Xylyl-18-crown-5 (6b): The ^1H NMR spectrum (250 MHz) is identical with that of **6a** except for the absence of the aryl-H (2) signal. The ^{13}C NMR spectrum is identical with that of **6a** except for the signal of aryl-C (2), which is now a triplet (δ 126.0, t, $^1J(CD)$ = 23 Hz, 1 C) of low intensity. GCMS mass spectrum: m/z (rel intensity) 297 (3, $M^{\bullet+}$, $C_{16}H_{23}O_5D$), 177 (15, $C_8H_{17}O_4$), 133 (8, $C_{16}H_{13}O_3$), 120 (8, C_8H_6OD), 118 (8, C_8H_4OD?), 105 (50, C_8H_7D), 89 (47, $C_4H_9O_2$), 79 (13, C_6H_5D), 45 (100, C_2H_5O).

[2-^{2}H]-1-(7-Hydroxy-2,5-dioxaheptyl)-3-(4-hydroxy-2-oxabutyl)-benzene (7b): ^1H NMR (250 MHz) δ 2.60 (br s, 1 H, OH), 2.79 (br s, 1 H, OH), 3.58–3.77 (m, 12 H, C_2H_4), 4.56 (s, 2 H, aryl-CH_2), 4.58 (s, 2 H, aryl-CH_2), 7.24 (d, ^3J = 6.0 Hz, 2 H, aryl-H(4, 6)), 7.29–7.36 (m, 1 H, aryl-H(5)). Two similar reaction mixtures, prepared with coarse magnesium and titrated to show a quantitative conversion of **4** to "basic" and "total" magnesium, were stored several months before quenching with D_2O as described. Product analysis with ^1H NMR (90 MHz) gave the following results: reaction A, **6a** 41%, **6b** 22%, **7b** 37%; reaction B, **6a** 42%, **6b** 21%, **7b** 37%.

Derivatization with Chlorotrimethylstannane. This reaction has been carried out twice, at room temperature and at 50 °C with aliquots from the same Grignard solution. A sample of the crude Grignard solution (5–10 mL), prepared from **4** in a sealed glass vessel as described above, was added to an excess (5-fold) of Me_3SnCl, using high-vacuum techniques. After 1 week, the ampule was opened and the solvent evaporated to dryness. To the residue CH_2Cl_2/H_2O was added. The organic phase

was dried ($MgSO_4$) and evaporated to dryness and the residue analyzed by 90 MHz ^1H NMR. It contained only two products, **6a** and 1-(2,5-dioxahept-6-enyl)-3-(7-hydroxy-2,5-dioxaheptyl)-2-(trimethylstannyl)-benzene (**14**). The 90-MHz ^1H NMR data of **14** could be derived in part from the spectrum of the mixture of **6a** and **14**: δ 0.35 (s, ^2J(SnH) = 54.6, 52.2 Hz, 9 H, Me), 4.01 (dd, ^3J(cis) = 7 Hz, ^2J(gem) = 2 Hz, 1 H, vinyl-H), 4.56 (s, 4 H, aryl-CH_2), 6.50 (dd, ^3J(trans) = 14 Hz, ^3J(cis) = 7 Hz, 1 H, O—CH=), 7.12–7.33 (m, 3 H, aryl-H). Similar treatment of a sample of crude **2** with Me_3SnCl for 3 h at 50 °C gave three products: **6a**, **11**, and **14** in yields of 46%, 17%, and 39%, respectively, according to the 90-MHz ^1H NMR spectrum. Only **11** was isolated by column filtration over Al_2O_3 (elution with Et_2O); it crystallized from Et_2O at −20 °C to give colorless crystals, mp 42–43 °C.

2-(Trimethylstannyl)-1,3-xylyl-18-crown-5 (11): ^{1}NMR (250 MHz) δ 0.37 (s, ^2J(SnH) = 54.9 and 52.6 Hz, 9 H, Me), 3.43–3.48 (m, 8 H, C_2H_4), 3.51–3.60 (m, 8 H, C_2H_4), 4.16, 4.97 (AB, ^2J(AB) = 12.1 Hz, 4 H, aryl-CH_2), 7.15–7.18 (m, 3 H, aryl-H). ^{13}C NMR (62.89 MHz) δ −4.6 (q, ^1J = 128 Hz, ^2J(SnC) = 355, 339 Hz, 3 C, Me), 68.6 (t, ^1J = 141 Hz, 2 C, CH_2), 69.9 (t, ^1J = 141 Hz, 2 C, CH_2), 70.2 (t, ^1J = 141 Hz, 2 C, CH_2), 70.4 (t, ^1J = 140 Hz), 2 C, CH_2), 74.8 (t, ^3J = 141 Hz, ^2J(SnC) = 22 Hz, 2 C, aryl-CH_2), 127.2 (d, ^1J = 160 Hz, ^4J(SnC) = 9 Hz, 1 C, aryl-C(5)), 128.6 (d, ^1J = 157 Hz, ^3J(SnC) = 40 Hz, 2 C, aryl-C(4, 6)), 143.9 (s, 1 C, aryl-C–Sn), 146.4 (s, ^2J(SnC) = 27.2 Hz, 2 C, aryl-C(1,3)). Mass spectrum (direct inlet, recorded on a Varian Mat CH5-DF spectrometer at 70 eV): m/z (rel intensity) 445 (100, $M^{\cdot+}$ − CH_3), 415 (14, $M^{\cdot+}$ — $3CH_3$), 269 (7, $C_{10}H_{13}OSn$), 253 (6, $C_{10}H_{13}Sn$), 239 (11, C_8H_7OSn), 223 (5, C_8H_7Sn), 165 (18, C_3H_9Sn), 133 (12, $C_6H_{13}O_3$), 119 (18, C_8H_7O), 105 (20, C_8H_9), 45 (30, C_2H_5O).

Reaction of 4 with Magnesium in [$^2H_8$]THF. In a high-vacuum dried sealed glass apparatus, a few milligrams of **4** were reacted with an excess of finely divided magnesium in [$^2H_8$]THF (300 μL). After stirring for 1 week, the solution was decanted into a 5-mm NMR tube connected by a capillary and sealed. According to ^1H NMR spectroscopy (90 MHz), **4** had reacted completely. The NMR tube was opened and quenched with H_2O. The organic material was isolated by extraction with CH_2Cl_2 and analyzed by GCMS. The gas chromatogram showed only one component, identical with pure **6a**, without any deuterium incorporation (the ether cleavage products, which must also have been present, do not pass the GC column).

Derivatization with D_2O. A solution of crude **2**, prepared as described above, was quenched with D_2O and evaporated to dryness. The residue was dissolved in H_2O/CH_2Cl_2. Acid was carefully avoided, and the workup was performed as quickly as possible. The organic layer was dried ($MgSO_4$) and evaporated, and the residue was dissolved in $CDCl_3$. The presence of a vinylic ether group in the cleavage product **12b** was derived from the ^1H NMR spectrum (90 MHz). The vinylic ether group disappeared when isolation by column chromatography (Al_2O_3) was attempted. [2-^{2}H]1-(2,5-dioxahept-6-enyl)-3-(7-hydroxy-2,5-dioxaheptyl)benzene (**12b**): ^1H NMR (90 MHz, incomplete data): δ 4.57 (s, 4H, aryl-CH_2), 6,50 (dd, ^{3}J(trans) = 14 Hz, ^{3}J(cis) = 7 Hz, 1H, O-CH=).

Conversion of 7b to [2-^{2}H]-1-(2,5-Dioxahexyl)-3-(2,5,8-trioxanonyl)-benzene (8b). To a suspension of KH (10 mmol, washed paraffin free with dry benzene) in dry benzene (50 mL) was added under stirring at room temperature a solution of **7b** (0.38 g, 1.4 mmol, as obtained chromatographically) in dry benzene (25 mL) within 5 min; a sticky precipitate formed. After stirring for another 15 min, methyl iodide (1.4 g, 10 mmol) was added at once. Stirring was continued for 20 min, H_2O was added, and the benzene was removed by evaporation. To the residue, CH_2Cl_2/H_2O was added; the organic phase was separated and dried ($MgSO_4$) and the solvent evaporated. The residue was a colorless oil consisting of **8b** (GCMS, Table I: 92%). A pure sample was obtained by preparative GC on a 10% OV 101 column, length 3 m, inside diameter 0.4 cm, at 220 °C.

8b: ^1H NMR (400 MHz) δ 3.390 (s, 3 H, OCH_3), 3.399 (s, 3 H, OCH_3), 3.556–3.701 m, 12 H, C_2H_4), 4.569 (s, 2 H, aryl-CH_2), 4.574 (s, 2 H, aryl-CH_2), 7.270–7.329 (m, 3 H, aryl-H). ^{13}C NMR (62.89 MHz) δ 58.9 (q, ^1J = 141 Hz, 2 C, OCH_3), 69.2 (t, 1 C, CH_2), 69.4 (t, 1 C, CH_2), 70.4 (t, 1 C, CH_2), 70.5 (t, 1 C, CH_2), 71.8 (t, 2 C, CH_2), 73.0 (t, 1 C, CH_2), 73.0 (t, 1 C, CH_2) [all triplets had ^1J = 152 Hz], 126.8 (d, ^1J = 160 Hz, 2 C, aryl-C(4,6)), 128.3 (d, ^1J = 160 Hz, 1 C, aryl-C(5)), 138.1 (s, 1 C, aryl-CH_2), 138.2 (s, 1 C, aryl-CH_2).

Reference Mixture Containing 1-(2,5-Dioxahexyl)-3-(2,5,8-trioxanonyl)benzene (8a). Under nitrogen, a mixture of ethyleneglycol monomethyl ether (methyl cellosolve, 12 mmol, 0.91 g) and diethyleneglycol monomethyl ether (methyl carbitol, 12 mmol, 1.44 g) in benzene (50 mL) was added to a stirred suspension of KH (30 mmol, washed paraffin-free) in dry benzene (25 mL). After 25 min, 1,3-bis(bromomethyl)benzene (2.6 g, 10 mmol) was added as such. Stirring was continued for 2 h, and the reaction mixture was quenched with H_2O. The organic material was isolated by benzene/H_2O extraction and the solvents removed by evaporation under reduced pressure. The residue (2.8 g, light yellow liquid) contained three products (characterization by ^1H NMR (90 MHz) and GCMS): 1,3-bis(2,5-dioxahexyl)benzene (**9a**), 1-(2,5-dioxahexyl)-3-(2,5,8-trioxanonyl)benzene (**8a**), and 1,3-bis(2,5,8-trioxanonyl)benzene (**10a**) in relative amounts of 21%, 38%, and 41%, respectively. The mass spectra of these compounds were compared with the data of **8b** and **9b**. There is a close resemblance between the mass spectra of **8a**/**8b** and **9a**/**9b** (see Table II).

Table II. GCMS Mass-Spectral Data of Compounds **8a**, **8b**, **9a**, **9b**, and **10a**: Relative Abundance of the Fragment[a]

fragment m/z	elem comp	educt 8a	8b	9a	9b	10a
266	$C_{15}H_{22}O_4$	0.0	0.7 D[b]	0.0	0.0	0.0
254	$C_{14}H_{22}O_4$	0.0	0.0	0.2	0.0	0.0
222	$C_{13}H_{19}O_3$	11.5	12.2 D	0.0	0.0	12.5
178	$C_{11}H_{14}O_2$	6.7	6.4 D	51.1	28.5 D	0.0
119	C_8H_7O	11.0	12.2 D	19.3	12.8 D	7.8
105	C_8H_9	64.8	75.5 D	89.7	77.1 D	50.0
103	$C_5H_{11}O_2$	64.8	75.5	12.8	16.5	72.3
91	C_7H_7	6.3	5.9 D	9.6	6.3 D	3.8
78	C_6H_6	8.1	8.3 D	11.2	11.0 D	6.3
59	C_3H_7O	100.0	100.0	100.0	100.0	100.0
45	C_2H_5O	30.4	33.1	50.0	50.0	23.4
expected $M^{+/c}$		298	299	254	255	342

[a] Intensities are given in %. [b] The fragments of **8b** and **9b** marked by D contain deuterium and have a m/z one unit higher. [c] The molecular ion of this type of compound has a very low intensity, its signal could only be detected from **9a** (m/z 254, 0.2%).

Reaction of 3 with Magnesium in THF. This reaction has been performed twice at different concentrations. Both reactions were carried out in an evacuated, fully sealed glass apparatus.

(a) In Dilute Solution. Compound **3** (1.3 g, 4.0 mmol) and magnesium (2.4 g, 100 mmol) were stirred at room temperature in dry THF (100 mL). Gradually, a colorless precipitate formed. After stirring for several days, the precipitate was allowed to settle and the clear supernatant was decanted into a second vessel; by distilling back part of the THF, the precipitate was washed. Both vessels were disconnected by sealing off at a capillary. Titration of an aliquot revealed that the clear solution contained 2.4 mmol of both "basic" and "total" magnesium, corresponding to 60% of **3**. The solution was quenched with D_2O and evaporated to dryness. After adding an aqueous NH_4Cl solution, the organic material was isolated by extraction with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and evaporated to dryness and the residue investigated by ^1H NMR and GCMS; it contained only a small amount of [2-^{2}H]-1,3-xylyl-15-crown-4 (**5b**). The solid precipitate was found to be pure **1** (40% yield; titration gave "basic" Mg: "total" Mg = 1:1); pure deuteriated **5b** was isolated after quenching with D_2O. The solubility of **1** in THF was 3.4 mmol/L.

[2-^{2}H]-1,3-Xylyl-15-crown-4 (5b): ^1H NMR (250 MHz) δ 3.70 (s, 8 H, C_2H_4), 3.71 (s, 4 H, C_2H_4), 4.63 (s, 4 H, aryl-CH_2) 7.05 (d, ^3J = 8 Hz, 2 H, aryl-H(4,6)), 7.22 (t, ^3J = 8 Hz, 1 H, aryl-H(5)). ^{13}C NMR (62.89 MHz) δ 69.6 (t, ^1J = 141 Hz, 2 C, CH_2), 70.3 (t, ^1J = 141 Hz, 2 C, CH_2), 70.6 (t, ^1J = 141 Hz, 2 C, CH_2), 72.2 (t, ^1J = 141 Hz, 2 C, aryl-CH_2), 125.8 (d, ^1J = 157 Hz, 2 C, aryl-C(4,6)), 127.6 (d, ^1J = 160 Hz, 1 C, aryl-C(5)), 128.3 (t, ^1J(CD) = 70 Hz, 1 C, aryl-C(2)), 139.1 (s, 2 C, aryl-C(1,3)). GCMS: m/z (rel intensity) m/e 253 ($M^{\cdot+}$, 7), 133 ($C_6H_{13}O_3$,35), 118 (C_6H_8O, 11), 105 (C_8H_7D, 100), 89 ($C_4H_9O_2$, 37), 79 (C_6H_5D, 9).

(b) In Concentrated Solution. Compound **3** (6.6 g, 20 mmol) was stirred with magnesium (2.4 g, 100 mmol) in dry THF (100 mL) for several days. A large amount of a white solid was formed; it precipitated when the stirring was stopped. The clear supernatant was decanted into a second vessel, and the residue (**1** and magnesium) was washed with some THF distilled back. Both vessels were disconnected by sealing off at a capillary. Titration of the clear solution (the fraction containing the side products) showed that it contained only 4 mmol of "basic" and "total" magnesium. The yield of solid **1** thus was about 80%. The fraction containing the side products was divided into four samples (sealed glass ampules) for characterization reactions (vide infra). Compound **1** was separated from the excess magnesium by decanting **1** as a slurry in THF from the metal pieces; it was crystallized by slowly concentrating a saturated THF solution. In this way crystals suitable for X-ray structure analysis could be obtained. A ^1H NMR spectrum of **1** was obtained from a saturated solution of the crystallized compound in [$^2H_8$]THF in a sealed glass apparatus (because of it's low solubility, **1** had to be washed thoroughly with the [$^2H_8$]THF by back-distillation to

remove all **6a**). 2-(Bromomagnesio)-1,3-xylyl-15-crown-4 (**1**): ^{1}H NMR (250 MHz) δ 3.95, 4.05 (2 × A_2B_2, ^3J = 13 Hz, 8 H, CH_2(6,7,12,13)), 4.05 (s, 4 H, CH_2(9,10)), 4.66 (s, 4 H, aryl-CH_2), 6.78 (d, ^3J = 7 Hz, 2 H, aryl-H(4,6)), 6.89 (t, ^3J = 7 Hz, 1 H, aryl-H(5)).

(c) Characterization of Side Products from Reaction b by a D_2O Quench. An ampule containing the soluble side products was quenched with D_2O. After evaporation to dryness and addition of aqueous HCl, the organic material was isolated by extraction with CH_2Cl_2. The organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness. The crude residue was treated with KH and MeL as described for the conversion of **7b** to **8b**. Analysis of the crude reaction mixture with ^{1}H NMR (90 MHz) and GCMS showed the presence of three components: **5a**, **5b**, and [2-^{2}H]-1,3-bis(2,5-dioxahexyl)benzene (**9b**: for mass spectrum see Table II).

(d) Characterization of Side Products from b with Chlorotrimethylstannane. An ampule containing the side products from the reaction of **3** with magnesium (vide infra) was treated with an excess of Me_3SnCl, using high-vacuum techniques. After standing for 1 day, the reaction mixture was quenched with D_2O and worked up by extraction with $CH_2Cl_2/H_2O/NH_4Cl$. After the usual workup, a mixture of **5a** and **17** (90-MHz ^{1}H NMR spectrum) was separated by column chromatography (Al_2O_3). 1-(4-Hydroxy-2-oxabutyl)-3-(2,5-dioxahept-6-enyl)-2-(trimethylstannyl)benzene (**17**) was characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. **17**: ^{1}H NMR (250 MHz) δ 0.36 (s, ^2J(SnH) = 54, 53 Hz, 9 H, Me), 3.55, 3.85 (A_2B_2, ^3J = 5 Hz, 4 H, OC_2H_4OH), 3.62–3.79 (A_2B_2, 4H, OC_2H_4O-vinyl), 4.02 (dd, ^3J(cis) = 7 Hz, ^2J(gem) = 2 Hz, 1 H, =CH_2Z), 4.21 (dd, ^3J(trans) = 14 Hz, ^2J(gem) = 2 Hz, 1 H, =CH_2E), 4.57 (s, 2 H, aryl-CH_2), 4.59 (s, 2 H, aryl-CH_2), 6.47, 6.53 (dd, ^3J(trans) = 14 Hz, ^2J(cis) = 7 Hz, 1 H, OCH=), 6.21–7.35 (m, 3 H, aryl-H). ^{13}C NMR (62.59 MHz) δ −5.0 (q, ^1J = 128 Hz, ^2J(SnC) = 355 Hz, ^2J(SnC) = 338 Hz, 3 C, Me), 61.6 (t, ^1J = 143 Hz, 1 C, CH_2), 67.2 (t, ^1J = 144 Hz, J(SnC) = 21 Hz, 1 C, CH_2), 68,3 (t, ^1J = 144 Hz, 1 C, CH_2), 71.3 (t, ^1J = 140 Hz, 1 C, CH_2), 75.2 (t, ^4J(SnC) = 25 Hz, 2 C, aryl-CH_2), 86.6 (ddd, ^1J = 161 Hz, ^1J = 156 Hz, ^2J = 9 Hz, 1 C, =CH_2), 126.4 (d, ^1J = 164 Hz, 1 C, aryl-C(5)), 128.2 (d, ^1J = 128 Hz, 1 C, aryl-C), 128.3 (d, ^1J = 168 Hz, J(SnC) = 35.0 Hz, 1 C, aryl-C), 142 (s, 1 C, aryl-(C-2)), 145.3 (s, 1 C, aryl-CCH_2), 145.4 (s, 1 C, aryl-CCH_2), 152 (d, ^1J = 182 Hz, OCH=).

(e) Characterization of Side Products from Reaction b with Methyl Iodide. Using sealed glass techniques, an ampule containing the side products was treated with an excess of methyl iodide. After 4 days at room temperature, a crystalline material had deposited. The reaction vessel was opened and the reaction mixture was quenched with D_2O. After evaporating to dryness, CH_2Cl_2 and brine were added, followed by extraction with CH_2Cl_2. The organic phase was dried ($MgSO_4$) and evaporated to dryness and the residue was subjected to column chromatography (Al_2O_3, Et_2O/THF gradient elution); **5a** and **18** (present in a ratio 1:1) were eluted in this order. 1-(4-Hydroxy-2-oxabutyl)-3-(2,5-dioxahept-6-enyl)-2-methylbenzene (**18**): ^{1}H NMR (250 MHz) δ 2.33 (s, 3 H, aryl-CH_3), 3.62, 3.88 (A_2B_2, ^3J = 5 Hz, 4 H, CH_2), 3.72–3.80 (A_2B_2, 4 H, CH_2), 4.02 (dd, ^3J(cis) = 7 Hz, ^2J(gem) = 2 Hz, 1 H, vinyl-H), 4.25 (dd, ^3J(trans) = 14 Hz, ^2J(gem) = 2 Hz, 1 H, vinyl-H), 4.59 (s, 2 H, aryl-CH_2), 4.61 (s, 2 H, aryl-CH_2), 7.17 (t, ^3J = 8 Hz, 1 H, aryl-H(5)), 7.30–7.33 (dm, ^3J = 7 Hz, 2 H, aryl-H(4,6)).

Reaction of Bromobenzene with Magnesium in the Presence of 1. In sealed glass apparatus, bromobenzene (4.5 g, 3 mL, 29 mmol) and magnesium (2.4 g, 100 mmol) were stirred in THF (180 mL) in the presence of **1** (about 3 mmol, as a suspension). In order to prevent a too vigorous reaction, the bromobenzene was added in small portions during several days. When all the bromobenzene had been added, the solid **1** had dissolved. The reaction vessel was opened and the reaction mixture carefully quenched with D_2O. After evaporating to dryness, CH_2Cl_2 and aqueous NH_4Cl were added. After a thorough extraction with CH_2Cl_2, the organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness. According to its ^{1}H NMR spectrum (90 MHz) the oily residue was essentially pure **25b**, no trace of **5a** or **5b** was present. [2-^{2}H]-1-(2,5-Dioxahept-6-enyl)-3-(4-hydroxy-2-oxabutyl)benzene (**25b**): ^{1}H NMR (250 MHz) δ 3.60–3.82 (m, 6 H, 3 × CH_2), 3.85–3.90 (m, 2 H, CH_2), 4.03 (dd, ^3J(cis) = 7 Hz, ^2J(gem) = 2 Hz, 1 H, =CH_2E), 4.20 (dd, ^3J(trans) = 14 Hz, ^2J(gem) = 2 Hz, 1 H, =CH_2Z), 4.58 (s, 2 H, aryl-CH_2), 4.61 (s, 2 H, aryl-CH_2), 6.54 (dd, ^3J(trans) = 14 Hz, ^3J(cis) = 7 Hz, 1 H, OCH=), 7.20–7.35 (m, 3 H, aryl-H). Without further purification, **25b** was converted to its methyl ether **26b** by reaction with KH and methyl iodide, using the procedure described for **8b**. The crude product was characterized by its ^{1}H and ^{13}C NMR spectrum and by GCMS. It contained 83% of **26b** and 17% of **9b** (GCMS). [2-^{2}H]-1-(2,5-Dioxahept-6-enyl)-3-(2,5-dioxahexyl)benzene (**26b**): ^{1}H NMR (250 MHz) δ 3.41 (s, 3 H, OCH_3), 3.59–3.68 (A_2B_2, 4 H, CH_2), 3.70–3.74 and 3.86–3.90 (A_2B_2, 4 H, CH_2), 4.03 (dd, ^3J(cis) = 7 Hz, ^2J(gem) = 2 Hz, 1 H, vinyl-H), 4.20 (dd, ^3J(trans) = 14 Hz, ^2J(gem) = 2 Hz, 1 H, vinyl-H), 4.59 (s, 2 H, aryl-CH_2), 4.60 (s, 2 H, aryl-CH_2), 6.54 (dd, ^3J(trans) = 14 Hz, ^3J(cis) = 7 Hz, 1 H, vinyl-H), 7.27–7.37 (m, 3 H, aryl-H). ^{13}C NMR (62.89 MHz) δ 58.9 (q, ^1J = 141 Hz, 1 C, OMe), 67.3 (t, 1 C, CH_2), 68.4 (t, ^1J = 142 Hz, 1 C, CH_2), 69.3 (t, ^1J = 141 Hz, 1 C, CH_2), 71.9 (t, ^1J = 144 Hz, 1 C, CH_2), 73.1 (t, 2 C, aryl-CH_2), 86.6 (ddd, ^1J = 161 Hz, ^1J = 156 Hz, ^2J = 10 Hz, 1 C, =CH_2), 126.9 (d, ^1J = 158 Hz, 1 C, aryl-C(5)), 128 (d, ^1J = 160 Hz, 2 C, aryl-C(4,6)), 138.0 (s, 1 C, aryl-CCH_2), 138.3 (s, 1 C, aryl-CCH_2), 151.7 (d, ^1J = 182 Hz, 1 C, OCH=). GCMS mass spectrum: m/z (rel intensity) 179 (2, $C_{11}H_{13}O_2D$), 136 (8), 120 (25, C_8H_6OD), 118 (20), 106 (100, C_8H_8D), 105 (49), 92 (14, C_7H_6D), 79 (17, C_6H_5D), 73 (15), 59 (99, C_3H_7O), 45 (51, C_2H_5O).

Control Experiments. Two experiments were carried out to verify that only the combination of the Grignard formation process and the activation by intramolecular coordination in **1** results in ether cleavage.

(a) Stability of 1 in the Presence of Phenylmagnesium Bromide. In a sealed glass apparatus, bromobenzene (4.5 g, 3 mL, 29 mmol) was reacted with magnesium (2.4 g, 100 mmol) in THF (180 mL). When the conversion of the bromobenzene was complete, **1** was added. The mixture was stored for 1 week before quenching with D_2O and worked up as described before. GCMS and ^{1}H NMR (90 MHz) showed that only **5b** was present; no traces of **5a** or **19** were found.

(b) Reaction of Bromobenzene with Magnesium in the Presence of 6a. In a 100-mL three-necked flask under nitrogen, magnesium (0.5 g, 20 mmol), dried THF (25 mL), and **6a** (0.59 g, 2 mmol) were placed. Bromobenzene (1.57 g, 10 mmol, in 25 mL of dried THF) was added within 2 h. After being stirred for another hour, the reaction mixture was quenched with D_2O. After the mixture was evaporated to dryness, CH_2Cl_2 and aqueous NH_4Cl were added. After extraction with CH_2Cl_2, the organic phase was dried ($MgSO_4$) and evaporated to dryness. The starting material **6a** (0.59 g, ^{1}H NMR 90 MHz) was recovered quantitatively.

Structure Determination and Refinement of 1. A colorless plate shaped crystal suitable for an X-ray structure determination was mounted under nitrogen in a Lindemann-glass capillary and transferred to an Enraf-Nonius CAD-4F diffractometer for data collection. Crystal data and details of the structure determination are given in Table II. Unit cell parameters were determined from a least-squares treatment of the setting angles of 10 reflections in the range $8.6 < \theta < 13.0°$. The monoclinic unit cell was checked for the presence of higher lattice symmetry.[18] Data were collected for one hemisphere [$-14 \le h \le 14$; $0 \le k \le 18$; $-13 \le l \le 13$] and corrected for Lp, absorption (Gaussian integration, grid 6

Table III. Crystal Data and Details of the Structure Determination of **1**

(a) Crystal Data	
formula	$C_{14}H_{19}O_4MgBr$
mol wt	355.51
crystal system	monoclinic
space group	$P2_1/n$ (Nr. 14)
a, b, c (Å)	11.099 (5), 14.132 (7), 10.113 (6)
β (°)	100.80 (5)
V (Å^3)	1558 (1)
Z	4
D_{calcd} (g cm^{-3})	1.516
F(000)	728
μ(Mo Kα) (cm^{-1})	26.6
crystal size (mm)	0.63 × 0.38 × 0.13
(b) Data Collection	
θ_{min}, θ_{max} (deg)	1.44, 27.5
radiation	Mo Kα (Zr-filtered), 0.71073 Å
$\omega/2\theta$ scan (deg)	1.00 + 0.35 tan θ
horizontal and vert. aperture (mm)	3.0, 5.0
distance from crystal to detector (mm)	173
reference reflections	02$\bar{1}$; 220; 20$\bar{2}$
total data	7447
total unique data	3585
obsd data ($I > 3.0\sigma(I)$)	1184
(c) Refinement	
no. of refined parameters	182
weighting scheme	$w = 1.0/[\sigma^2(F) + 0.002074F^2]$
final R, wR, S	0.0691, 0.0862, 1.95
$(\Delta/\sigma)_{max}$ in final cycle	0.0299

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Table IV. Fractional Atomic Coordinates and Equivalent Isotropic Thermal Parameters with Esd's in Parentheses for **1**

	x	y	z	U_{eq},[a] (Å^2)
Br	0.4480 (1)	0.1599 (1)	0.2193 (1)	0.0810 (5)
Mg	0.2519 (3)	0.0687 (3)	0.2106 (3)	0.058 (1)
O(1)	0.157 (1)	0.1157 (7)	−0.0043 (9)	0.094 (4)
O(2)	0.2814 (8)	−0.0338 (7)	0.065 (1)	0.086 (4)
O(3)	0.3249 (8)	−0.0526 (7)	0.321 (1)	0.091 (4)
O(4)	0.246 (1)	0.0898 (8)	0.4541 (9)	0.104 (5)
C(1)	0.079 (1)	0.1204 (8)	0.231 (1)	0.062 (4)
C(2)	0.002 (1)	0.1580 (9)	0.113 (2)	0.090 (8)
C(3)	−0.100 (2)	0.205 (1)	0.122 (3)	0.15 (1)
C(4)	−0.131 (2)	0.223 (1)	0.236 (3)	0.15 (1)
C(5)	−0.066 (2)	0.189 (1)	0.363 (2)	0.128 (8)
C(6)	0.044 (1)	0.138 (1)	0.353 (2)	0.083 (6)
C(7)	0.030 (2)	0.142 (1)	−0.019 (2)	0.103 (8)
C(8)	0.188 (2)	0.056 (1)	−0.111 (1)	0.122 (8)
C(9)	0.297 (2)	0.004 (1)	−0.056 (2)	0.12 (1)
C(10)	0.373 (2)	−0.101 (1)	0.116 (2)	0.116 (8)
C(11)	0.337 (2)	−0.135 (1)	0.245 (2)	0.118 (8)
C(12)	0.303 (2)	−0.071 (1)	0.453 (2)	0.14 (1)
C(13)	0.319 (2)	0.017 (2)	0.527 (2)	0.14 (1)
C(14)	0.124 (2)	0.099 (1)	0.475 (2)	0.109 (8)

[a] $U_{eq} = 1/3\sum_i\sum_j U_{ij}a_i^*a_j^*a_i a_j$.

× 12 × 16; max and min correction, 2.787 and 1.381), and for a linear decay of 22% during the 154 h of X-ray exposure time. The reflections were measured at ψ values calculated with the A-vector method[19] in order to minimize the observed splitting of the reflection profiles. Standard deviations based on counting statistics were increased according to an analysis of the excess variance of the three reference reflections: $\sigma^2(I) = \sigma^2_{cs}(I) + (0.026I)^2$.[20] The crystal was found to be poorly reflecting at higher θ values; this is caused by the high rigid body thermal motion of the molecules. The space group $P2_1/n$ was determined from the observed systematic extinctions: $h0l$; $h + l = 2n + 1$ and $0k0$, $k = 2n + 1$. The structure was solved with direct methods (SHELXS86);[21] the solution with the best figure of merit revealed all non-H atoms. Refinement of F was carried out by full-matrix least-squares techniques. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were introduced on calculated positions [d(C–H) = 0.98 Å] and included in the refinement riding on their carrier atom with one common isotropic thermal parameter [U = 0.16 (2) Å^2]. Weights were introduced in the final refinement cycles, and convergence was reached at R = 0.0691. A final difference Fourier synthesis reveals residual densities between 0.92 and −0.54 e/Å^3 near the Br atom which are interpreted as residual absorption artefacts. Final atomic coordinates and equivalent isotropic thermal parameters are listed in Table IV. Neutral atom scattering factors were taken[22] and corrected for anomalous dispersion.[23] Data collection was done with a modified CAD-4F software package.[24] Calculations were performed with SHELX76[25] and the EUCLID package[26] (geometrical calculations and illustrations) on a MicroVAX-II.

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Supplementary Material Available: Tables of anisotropic thermal parameters, all H-atom parameters, complete lists of bond lengths, bond angles, and a thermal motion ellipsoid plot (8 pages); listing of observed and calculated structure factor amplitudes (16 pages). Ordering information is given on any current masthead page.

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