of the solvent, the residue was recrystallized from chloroform–ethanol, white needles, mp 239° (lit.[27] 239–240°), 92% after recrystallization. The uv absorption spectrum agreed with that published for DPP.[9]

Techniques and apparatus used for voltammetry and coulometry have previously been described.[11,28] TFA was reagent grade and used without further purification. Reagent grade dichloromethane was passed through a column of neutral aluminum immediately before use. Reagent grade TPE was recrystallized before use.

Kinetics. Solutions of $TPE\cdot^+$ in the solvent system were prepared by partial oxidation at a low constant current (12.5 mA) of solutions of TPE. The concentration of both $TPE\cdot^+$ and TPE were determined by the magnitude of the limiting reduction and oxidation currents, respectively, at the rde. The concentration of $TPE\cdot^+$ was continuously monitored by the value of the limiting current at +0.8 V. The reaction cell was water jacketed and the temperature was controlled either by tap water or by a kyrostat (Ultra DK 80 DW). Second-order rate constants were calculated from plots of $1/[TPE\cdot^+]$ *vs.* time.

Acknowledgment. The assistance of Dr. Bo Svensmark Jensen in simulation of the steady-state cyclic voltammogram is greatly appreciated.

---

[27] A. Gatzke, R. A. Stairs, and D. C. M. Diaper, *Can. J. Chem.*, **46**, 3695 (1968).

[28] O. Hammerich and V. D. Parker, *J. Chem. Soc., Perkin Trans. 1*, 1718 (1972).

Complexation Kinetics of Dineopentylmagnesium with *l*-Sparteine

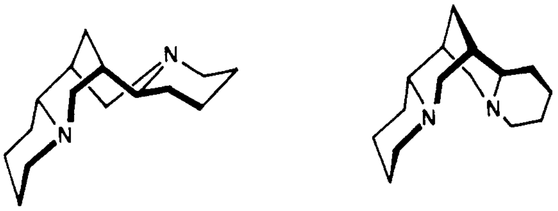
Gideon Fraenkel,* Bernard Appleman, and J. G. Ray

Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received February 26, 1974*

Abstract: The equilibrium between *l*-sparteine (Sp), dineopentylmagnesium, and the 1:1 complex $R_2Mg\cdot Sp$ in THF–dimethoxymethane has been characterized and the kinetics of ligand magnesium exchange were investigated with the techniques of nmr line-shape analysis. Rates of ligand exchange which turn out to be much slower than for other tertiary amines give rise to rate laws for the forward and reverse reaction whose molecularity is identical with that found on the left and right sides of reaction 1. At 60°, $1/\tau_{R_2Mg} = 32$ (Sp) and $1/\tau_{comp} = 10.4\ sec^{-1}$, and the corresponding Eyring activation parameters are $\Delta H^{\ddagger} = 20$ kcal/mol and $\Delta S^{\ddagger} = 8.2$ eu. These results on comparison to other work lead to the conclusion that the slow step in the exchange process involves a conformational inversion of sparteine in a monodentate 1:1 complex from cisoid to transoid, thus allowing the approach of ether to magnesium.

Primary organomagnesium compounds in solution at equilibrium undergo fast inversion at carbon bonded to metal,[1,2] carbon–metal bond exchange, and metal base (ether and amine) coordination exchange.[3,4] Ordinarily for primary organomagnesium compounds at −20 to 100° in the presence of ethers and tertiary amines only the inversion process is on the nmr time scale, and its mechanism has been studied with the methods of nmr line-shape analysis.[1,2] In contrast to inversion, both bond and coordination exchange are very much faster, too fast for nmr methods. These processes have so far eluded kinetic study and although various proposals have been made nothing is presently known about their mechanisms.

In this paper we present the first kinetic study of coordination exchange of an organomagnesium compound complexed to a tertiary amine.



1

For some time it has been apparent that *l*-sparteine[5] (**1**), an optically active, naturally occurring tertiary diamine, is an excellent ligand toward metal ions. For instance, periodically it is rediscovered that addition reactions of certain organometallic compounds carried out in the presence of sparteine result in products with different degrees of optical purity. These reactions include the metalation of isopropylferrocene by butyllithium,[6] the reactions of α-phenethyllithium,[7] butyllithium additions to carbonyl compounds,[7] the formation of allenes from *gem*-dibromocyclopropanes and butyllithium,[7] 1,4-addition reactions of Grignard reagents,[8] and the addition of the Reformatsky reagent to benzaldehyde.[9] The implication of these results is that *l*-sparteine, by complexing with the respective organometallic, imparts a chiral environment about the carbon–metal bond and thus induces asymmetry into the transition states for the different reactions.[5–9]

---

[1] M. Witanowski and J. D. Roberts, *J. Amer. Chem. Soc.*, **88**, 737 (1966).

[2] G. Fraenkel and T. D. Dix, *J. Amer. Chem. Soc.*, **88**, 979 (1966); G. Fraenkel, C. Cottrell, and D. T. Dix, *ibid.*, **93**, 1704 (1971).

[3] H. O. House, R. A. Latham, and G. M. Whitesides, *J. Org. Chem.*, **32**, 2481 (1967).

[4] See D. F. Evans and M. S. Khan, *Chem. Commun.*, 67 (1966); *J. Chem. Soc. A*, 1643, 1648 (1967); D. F. Evans and V. Fazakery, *Chem. Commun.*, 974 (1968); J. A. Magneson and J. D. Roberts, *J. Org. Chem.*, **37**, 133 (1972).

[5] *Chem. Abstr.*, **73**, Index Guide, 1641G (1970), dodecahydro-7,4-methano-2*H*,6*H*-dipyrido[1,2-*a*:1′,2′-*e*][1,5]diazocine.

[6] T. Aratani, T. Gonda, and N. Nozaki, *Tetrahedron*, **26**, 545 (1970).

[7] H. Nozaki, T. Aratani, T. Toraya, and R. Noyori, *Tetrahedron*, 27, 905 (1971).

[8] R. A. Kretchmer, *J. Org. Chem.*, **37**, 2744 (1972).

[9] M. Guette, J. P. Guette, and J. Capillon, *Tetrahedron Lett.*, 2863 (1971).

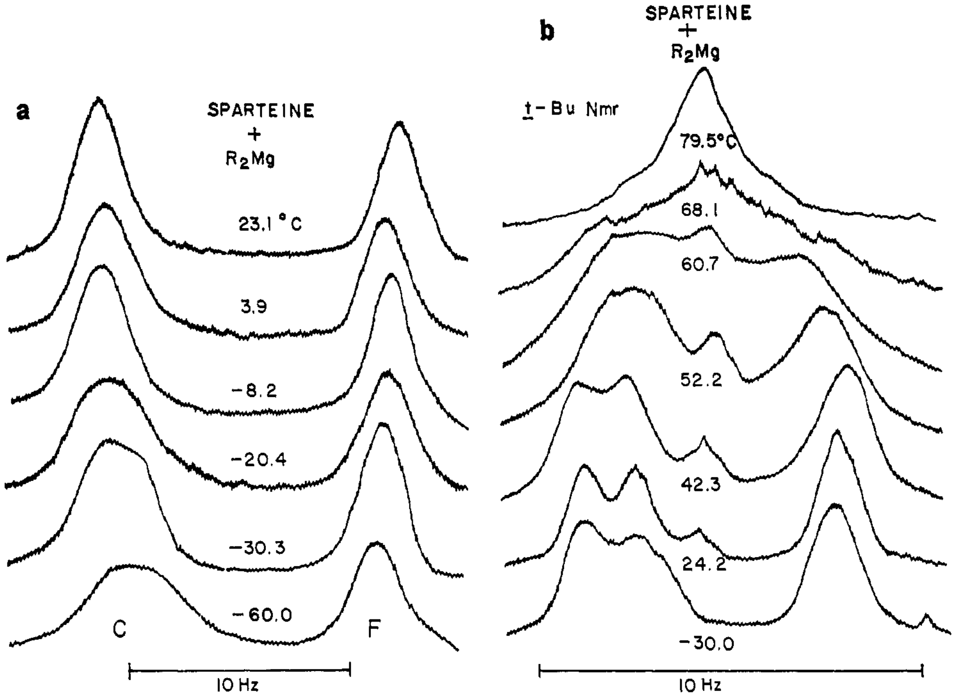
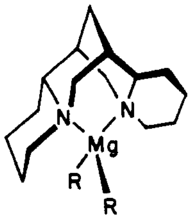


Figure 1. Nmr, 100 MHz, for a mixture containing dineopentylmagnesium and sparteine in 1:1 THF–dimethoxymethane, sample **3**, at different temperatures: (a) methylene hydrogens of R_2Mg; (b) *tert*-butyl hydrogens.

Actually a number of bidentate complexes of *l*-sparteine with nickel(II),[10] cobalt(II),[10] zinc(II),[10] manganese(II),[10] iron(II),[10] and magnesium(II)[11a,b] have been isolated and identified.

We have already reported how nmr studies of mixtures of *d*-bis(2-methylbutyl)magnesium with *l*-sparteine reveal the existence of a bidentate complex, with magnetically nonequivalent 2-methylbutyl groups (due to the skewed shape of the cisoid sparteine moiety),[12] **2**.



2

Interestingly in this complex, at room temperature inversion, bond exchange, and coordination exchange are all slow on the nmr time scale and this result contrasts starkly with the very fast processes observed for all other ethers and amines tried so far.[12] At higher temperatures there is some line broadening and coalescence indicative that one or more exchange processes are now on the nmr time scale. This observation provided us for the first time with the opportunity to study magnesium ligand exchange and disentangle its mechanism. In this work we have chosen to simplify the experimental problems by studying the system dineopentylmagnesium sparteine.

It will be shown below how we have purified dineopentylmagnesium such that impurities could not be detected with the nmr method. The equilibrium between sparteine and its dineopentylmagnesium complex has been characterized thermodynamically. Kinetics of exchange have been investigated and a mechanism is proposed to account for the unusually slow (compared to other amines) exchange processes. It is important to stress that this mechanism applies to a system at *equilibrium*.

Results and Discussion

Neopentylmagnesium chloride was converted into the mercury compound ($J(CH_3,{}^{199}Hg)$ = 5.9 Hz). Treatment of the mercury compound with powdered magnesium gave dineopentylmagnesium. Ordinarily four bond H,H couplings in neopentyl systems are generally too small to resolve and simply contribute to the line width. However, dilute samples of dineopentylmagnesium show fine structure; see Experimental Section, $J(CH_2,CH_3)$ = 0.35 Hz.

The addition of sparteine to a solution of dineopentylmagnesium in ethers below 30° gives rise to two closely spaced resonances deshielded with respect to the free organomagnesium compound. To avoid precipitation of solutes and viscosity problems we have chosen to employ a 50:50 mixture of THF–dimethoxymethane as solvent in these experiments. The three resonances each for the *tert*-butyl and methylene hydrogens in these solutes are reproduced in Figure 1. Notice that while the extra *tert*-butyl resonances are well resolved, those for the methylene hydrogens overlap considerably though two lines can be discerned from the shape of the absorption.

Careful comparison of peak areas together with the known concentrations of total sparteine and total dineopentylmagnesium (R_2Mg) in these samples establishes that this compound is in equilibrium with a 1:1

---

[10] S. F. Mason and R. D. Peacock, *J. Chem. Soc., Dalton Trans.*, 226 (1973).

[11] (a) P. West and M. C. Woodville, Proceedings, 4th International Conference on Organometallic Chemistry, July 28–August 1, 1969, p C15. (b) Sparteine is selectively absorbed by dry magnesium sulfate from ether solution: F. Oakes, Ohio State University.

[12] G. Fraenkel, C. Cottrell, J. G. Ray, and J. Russell, *Chem. Commun.*, 273 (1971).

Table I. Concentrations and Equilibrium Constants

$$R_2Mg + Sp \rightleftharpoons R_2Mg \cdot Sp$$

Sample no.	$[R_2Mg]_0$[a]	$[Sp]_0$	$[R_2Mg]_{eq}$	$[Sp\cdot]_{ep}$	$[Complex]_{eq}$	K_{eq} at 25°, l./mol
1	2.00	2.00	0.60	0.60	1.40	3.89
2	1.28	1.28	0.51	0.51	0.77	2.93
3	1.00	1.00	0.41	0.41	0.59	3.51
4	0.48	0.48	0.28	0.28	0.20	2.55
5	0.43	0.43	0.25	0.25	0.18	2.88
6	0.75	0.75	0.32	0.32	0.43	4.20
7	0.435	0.428	0.260	0.253	0.175	2.66
8	0.249	0.491	0.112	0.354	0.137	3.46

[a] Concentrations are in mol/l., 0, initial, eq, equilibrium.

complex containing sparteine (Sp) (see eq (1) and Table

$$R_2Mg + Sp \rightleftharpoons R_2Mg \cdot Sp \qquad (1)$$

$$R = \text{neopentyl}$$

$$K_{304} = 3.3 \pm 0.6\ M^{-1}$$

I). Thus the extra resonances at lower field are assigned to two nonequivalent alkyl groups on the 1:1 complex as has already been shown for the system bis(2-methylbutyl)magnesium–sparteine.[12] In that system, however, the equilibrium constants were too large to measure.

Equilibrium constants for reaction 1 were determined within the temperature range −30 to +30°. Under these conditions the spectra were not visibly perturbed by viscosity or exchange effects. The result of this experiment was that the equilibrium constant did not vary with temperature within experimental error. Assuming a maximum uncertainty of K_1 of *ca.* 20% we calculate the maximum value of ΔH to be +0.4 kcal/mol. This may be taken to be zero. With increasing temperature, above +30°, the nmr line shapes for the samples containing system 1 in 1:1 THF–dimethoxymethane exhibit progressive broadening and coalescence characteristic of an exchange process taking place on the nmr time scale; that is some process is responsible for exchanging neopentyl groups on the complex with those on solvent complexed dineopentylmagnesium (see Figure 1). Note that the coordination of these solvents to magnesium is not known.

The analysis of nmr line shapes for first-order exchanging systems is most efficiently handled with the Kubo–Anderson–Sack procedure.[13] The parameters required to calculate the nmr line shape are the shifts for the lines effected by exchange, their relative intensities, line-width parameters (to account phenomenologically for relaxation not caused by exchange) and the mean lifetime of the different species between successive exchanges, τ. Since these parameters are related to the rate law R for exchange, it can be appreciated that

$$1/\tau_{\text{species}} = R\ \text{exchange}/(\text{species}) \qquad (2)$$

some assumptions about the mechanism must be built into the equations for exchange. Thus if an exchanging system has as many as 16 species with different chemical shifts,[13] each giving rise to a single line, and there are exchange processes which cause the shift of any one species to average with that of any other, then by use of the above listed parameters in conjunction with now standard computer programs it is possible to calculate the nmr line shape for the system.[13]

Notice in the present work since we are dealing only with neopentyl groups, we need not be concerned with spin coupling since the methylene methyl coupling constant is in general too small to measure; it is responsible for the unusually broad line widths obtained in the methylene resonances.

We now describe how nmr line shapes have been simulated for reaction 1, that is the data illustrated in Figure 1. There are three neopentyl resonances and we propose that these represent two different neopentyls on the complex Ne_1 and Ne_2 and a third one on solvent complexed dineopentylmagnesium, Ne_s. From inspection of Figure 1 it is qualitatively apparent that there are three possible exchange processes taking place (eq 3–5).

$$Ne_1 \rightleftharpoons Ne_2 \qquad (3)$$

intracomplex neopentyl exchange

$$Ne_2 \rightleftharpoons Ne_s \qquad (4)$$

$$Ne_1 \rightleftharpoons Ne_s \qquad (5)$$

intermolecular neopentyl exchange

Neopentyl groups may exchange between the complexed and "free" environment (eq 4 and 5) and also perhaps the two neopentyl groups on the complex may exchange places (eq 3). Whether or not this intracomplex exchange contributes to the nmr line shape can be decided by inspection of the *tert*-butyl and methylene neopentyl resonances of the complex. The *tert*-butyl resonance consists of two distinct lines whose separation changes from 2 Hz at −50° to 1.5 Hz at room temperature with coalescence occurring around 50°. On the other hand, the methylene neopentyl resonance of the complex which shows two overlapping peaks between −50 and −30° narrows to a single line (width 2.1 Hz) on warming to room temperature. This behavior cannot be the result of some fast intracomplex exchange because at room temperature the *tert*-butyl resonance for the complex is still a well-defined doublet. Therefore it is more likely that the methylene line narrowing results from a decrease on warming in the intrinsic shift between the two methylenes in the complex.

The intrinsic nmr parameters used in the line-shape calculations were obtained as follows. The separation between the average neopentyl methylene resonance in the sparteine and solvent complexes was 12.50 Hz between −40 and +20° in the slow exchange region. Also the widths of the methylene resonances in the three environments did not vary within this temperature range—they were all 2.1 Hz. In contrast to these results the separation between the CH_2Mg resonances

---

(13) H. M. McConnell and C. H. Holm, *J. Chem. Phys.*, **28**, 430 (1958); P. W. Anderson, *J. Phys. Soc. Jap.*, **9**, 316 (1954); R. Kubo, *ibid.*, **9**, 935 (1954); R. A. Sack, *Mol. Phys.*, **1**, 163 (1958); M. Saunders, *Tetrahedron Lett.*, 1699 (1963). We thank Professor Martin Saunders, Yale University, for a copy of his computer program.

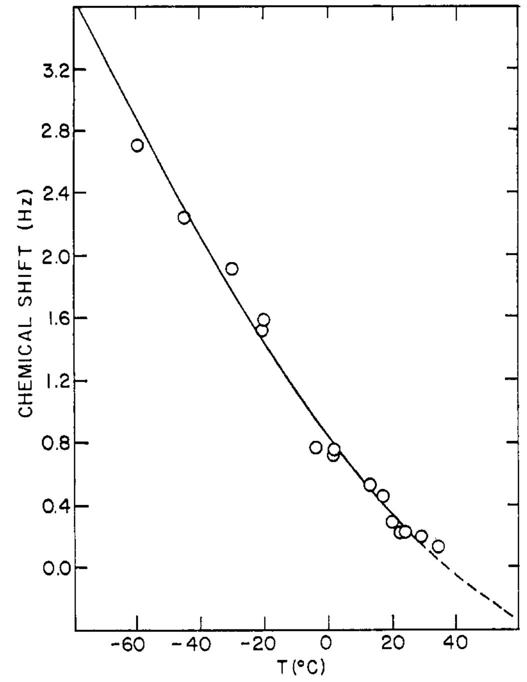


Figure 2. Temperature dependence of the chemical shift, 100 MHz, between the two CH_2Mg resonances in the dineopentylmagnesium·sparteine complex, sample **3**.

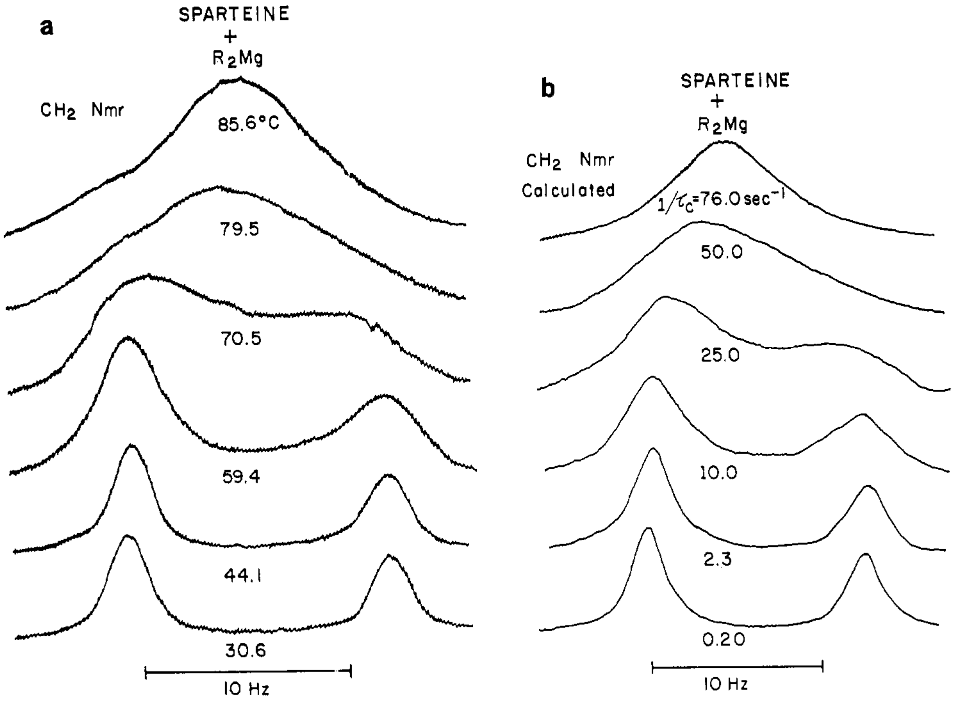


Figure 3. (a) Nmr, 100 MHz, line shapes for CH_2Mg absorption in sample **2** at different temperatures; (b) calculated CH_2Mg line shapes for sample at different values of τ_c.

on the complex varied with the temperature (see Figure 2). This is drawn on the assumption that significant exchange broadening occurs only above 30°, as explained above. Notice how this internal shift passes through zero around 25°. Calculations employing all three exchange processes, eq 3–5, using different ratios of $\tau_{4,5}$ to τ_3, inter- to intramolecular exchange, over a wide range of rates were tried. None of these results bore any resemblence to the experimental line shapes. In fact only when intracomplex exchange (3) is ignored entirely are the theoretical line shapes in accord with the observed ones. These calculated curves are displayed in Figure 3. Thus using these methods we cannot detect an independent intracomplex exchange of neopentyl groups.

Comparison of theoretical to experimental nmr line shapes yields values for $\tau(R_2Mg)$ and $\tau(R_2Mg{\cdot}Sp)$. Kinetic analysis of these results is accomplished by means of eq 2. There are several possible kinetic steps by which a neopentyl group could be transferred between R_2Mg and $R_2Mg{\cdot}Sp$ environments, for instance (1), (6), and (7). Any one, two, or some combination

$$\mathrm{Sp^* + R_2Mg{\cdot}Sp \rightleftarrows R_2Mg{\cdot}Sp^* + Sp} \qquad (6)$$

$$\mathrm{R_2^*Mg^* + R_2Mg{\cdot}Sp \rightleftarrows R_2^*Mg^*Sp + R_2Mg} \qquad (7)$$

$$\mathrm{Sp + R_2Mg} \underset{k_d}{\overset{k_f}{\rightleftarrows}} \mathrm{R_2Mg{\cdot}Sp} \qquad (1)$$

of all three might operate. To begin with we considered step 1 alone. The different mean lifetimes would be given by

$$1/\tau_{\mathrm{R_2Mg}} = k_f\,(\mathrm{Sp}) \qquad (8)$$

$$1/\tau_{\mathrm{R_2Mg \cdot Sp}} = k_d \qquad (9)$$

noting that $k_f/k_d = K$ the overall equilibrium constant. Actually the mean lifetime of the complex is indeed independent of all constituents while that for dineopentylmagnesium is proportional to the sparteine concentration (Figures 4 and 5). In fact the ratio of mean lifetimes $\tau_{\mathrm{R_2Mg \cdot Sp}}/\tau_{\mathrm{R_2Mg}}$ which fits the data is given by K(Sp). Typical results obtained for this system at 60° are listed in Table II.

Finally from the temperature dependence of the τ's using (8) and (9) we obtained the parameters of activation, averaged for all samples, listed at the end of Table II (see Figure 6). Noting that the heat of the associa-

Table II. Kinetic Parameters for Exchange[a]

$$R_2Mg + Sp \underset{k_d}{\overset{k_f}{\rightleftarrows}} R_2Mg\cdot Sp$$

Sample no.	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	E_a, kcal/mol	Log A	k_d, sec^{-1}	k_f, sec^{-1} M^{-1}	τ_c, sec	τ_{R_2Mg}, sec
1	20.2	+7.8	20.9	15.0	10.5	40.9	0.096	0.82
2	20.0	+7.2	20.7	14.9	10.3	30.2	0.097	0.13
3	19.9	+7.2	20.6	14.9	10.5	26.8	0.096	0.13
4	20.6	+9.0	21.2	15.2	10.3	29.7	0.097	0.27
7	18.4		19.1		9.8	26.1	0.1020	0.30
8	20.8	+9.9	21.5	15.4	11.0	38.1	0.091	0.15
Av value	20.0	8.2	20.65	15.0	10.4	32.0	0.097	
Std dev	0.9	1.2	0.85	0.3	0.4	6.1	0.0036	
Av dev	0.6	1.0	0.55	0.7	0.3	5.7	0.0025	

[a] The parameters are evaluated with respect to the decomposition of the complex.

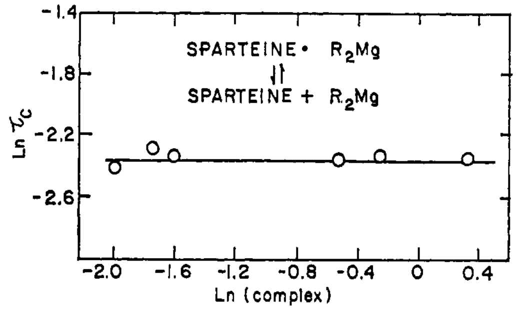


Figure 4. Kinetic plot for reaction 1, ln τ_c *vs.* ln ($Ne_2Mg\cdot Sp$).

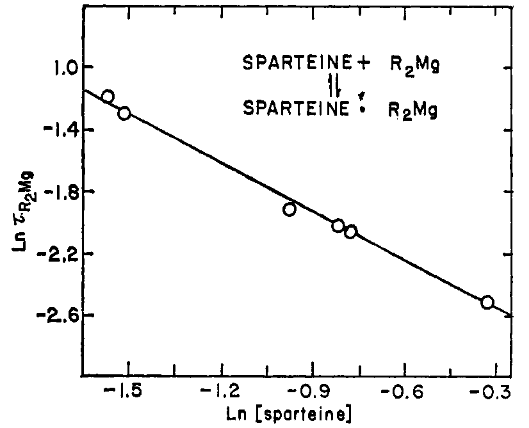


Figure 5. Kinetic plot for reaction 1, ln τ_{R_2Mg} *vs.* ln (Sp·).

tion of reaction 1 is close to zero we see how the transition state for exchange lies equidistant to both sides of the reaction.

Now it is worthwhile to discuss the mechanism of this exchange reaction. It seems unlikely that reaction 1 takes place in one kinetic step since two nitrogen–magnesium bonds[12] would have to be broken at the same time. Furthermore, were straight dissociation to take place, some of the complexes might undergo a partial dissociation where the dineopentylmagnesium moved a short distance (say 10 Å) from the sparteine, then returned with the alkyl groups reversed. Such a predissociative process should have the effect of averaging the chemical shifts of the neopentyl groups on the complex. But as mentioned in the foregoing discussion such an exchange process has not been detected. Therefore it is not likely that reaction 1 takes place in one step and the magnesium–nitrogen bonds must break one at a time.

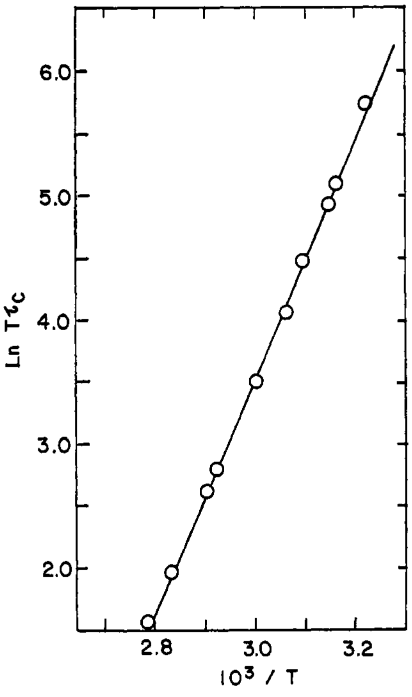
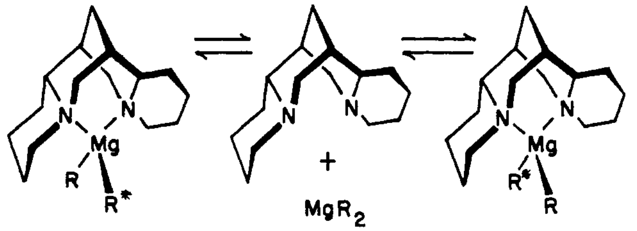
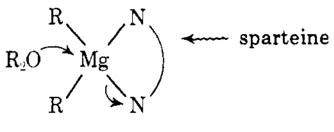


Figure 6. Eyring plot for sparteine exchange sample 3.



(10)

Overall, two coordinate bonds from magnesium to nitrogen become replaced by bonds from magnesium to oxygen. In the following scheme which is proposed to account for the observed behavior in reaction 1 magnesium–nitrogen and magnesium–oxygen coordination bonds are broken and formed, respectively, in alternate single steps. In principle, attack of ether on magnesium could be concerted with the departure of a nitrogen ligand. However, the sheer bulk of the



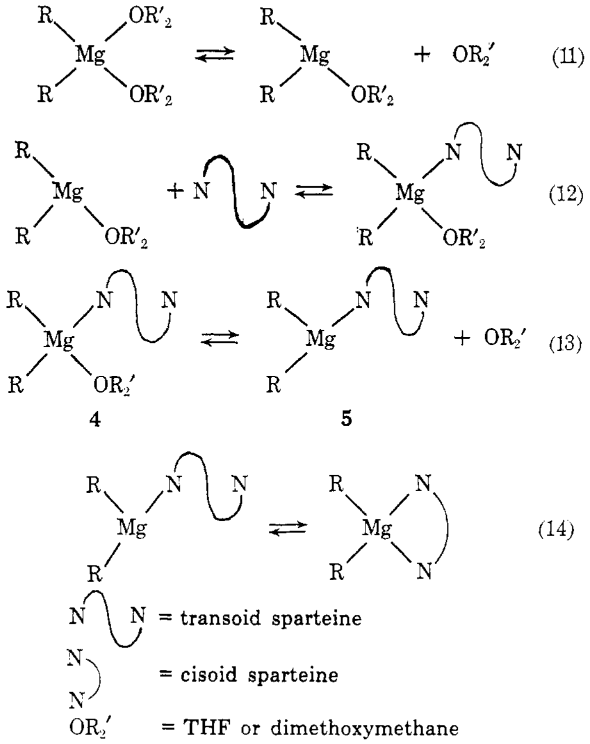
3

sparteine part of the caged complex should preclude the observation of such a step for steric reasons, *i.e.*, some other process will be faster.

It is assumed by analogy with previous reports, that dineopentylmagnesium is a monomer in the solvent system here.[1,14]

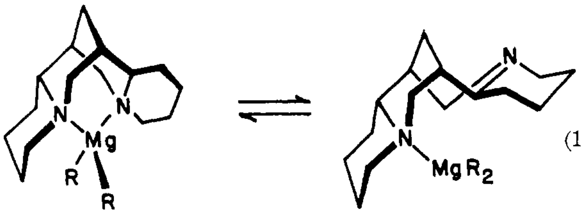
Since magnesium–THF and -dimethoxymethane coordination exchange is fast on the nmr time scale, the mode of coordination of these ethers to magnesium is not important for the purposes of this study. From crystallographic data it is reported that three or four THF molecules coordinate to magnesium[15] while the coordination behavior of dimethoxymethane is not known at all. In Scheme I, for convenience only, we depict two ether molecules per magnesium.

Scheme I



Free dialkylmagnesium is undoubtedly bound to solvent molecules, in our experiments to dimethoxymethane or THF or both. We envisage this species readily loses a solvent molecule and the resulting three coordinate magnesium then forms a new bond to nitrogen in transoid sparteine forming a mixed complex, **4**. The latter loses the second molecule of ether forming the tricoordinate 1:1 transoid complex, **5**. This finally undergoes a conformational inversion to cisoid product, eq 14.

We already know from qualitative experiments that the rate of exchange of dialkylmagnesium compounds between the dietherate and the *N,N,N',N'*-tetramethylethylenediamine complex is too fast to measure on the nmr time scale at 0°.[16] Then the feature responsible in the R_2Mg–sparteine system for such a slow rate of ligand exchange must have mainly something to do with the bulk of the sparteine. From inspection of Scheme I it would appear that steps (11), (12), and (13) should be fast. However, the last one (eq 14) involving a conformational cisoid ⇄ transoid inversion, could be the slow step of the exchange process. Recall that steric effects preclude an attack of ether on magnesium in the cisoid complex concerted with breaking the Mg–N bond. First, part of the sparteine has to move out of the way. The very large enthalpy of activation for the exchange process observed here is far more consistent with a conformational inversion than with any of the other steps proposed.



(15)

Sparteine has at various times been reported to exert profound physiological effects. Sparteine increases the toxic dose of potassium salts to induce fibrillation.[17] It has been used extensively to control arrhythmia especially in veterinary medicine[18] and to induce abortion in mammals.[19] Interestingly magnesium sulfate acts as a depressant of muscle activity in general.[20]

From the observations just mentioned together with complexation behavior of sparteine to organomagnesium compounds as well as magnesium sulfate described here it would seem attractive to speculate that the pharmacological effects of sparteine are related to its properties as a ligand including the slow exchange behavior. It may be that in exerting these unusual effects sparteine acts by perturbing the dynamic behavior of metal ions in muscle.

Thus in summary we have found out that for steric reasons the rate of ligand exchange of dineopentylmagnesium between its etherates and its sparteine complex is unusually slow compared to systems with other tertiary amines. We propose that the slow step in the exchange involves conformation changes in the sparteine. In contrast to this the equilibrium constants for the complexation of sparteine to magnesium and other amines to sparteine are quite similar. It is the dynamic behavior of the sparteine complexes which is unusual.

Experimental Section

Solvents. Pentane and diethyl ether were stored over lithium aluminum hydride and distilled immediately before use in a dry system.

Magnesium and *n*-octyl bromide were reacted in tetrahydrofuran (first distilled from calcium hydride) to produce 0.5–1.0 M solutions of the corresponding Grignard reagent. Tetrahydrofuran was distilled from this solution, under argon, when needed. An equivalent procedure was used to dry dimethoxymethane.

Apparatus and General Techniques. Samples in 8-mm o.d. tubes

---

[14] F. Walker and E. C. Ashby, *J. Amer. Chem. Soc.*, **91**, 3845 (1969).

[15] (a) M. C. Perucaud and M. T. LeBihan, *Acta Crystallogr., Sect. B*, **24**, 1502 (1968), $MgBr_2\cdot(THF)_4$; (b) M. Vallino, *J. Organometal. Chem.*, **20**, 1 (1969), $CH_3MgBr\cdot(THF)_3$.

[16] Dr. Simon Yu, private communication, The Ohio State University, 1972.

[17] F. D'Allaines, N. duBouchet, J. Voysse, B. Latschia, and C. Perrin, *Journees Therap.*, **8**, 259 (1953).

[18] E. Czarnecka, A. Kolinska-Marzcs, and A. Szadowska, *Acta Pol. Pharm.*, **24**, 545 (1967); F. Mercier, J. Mercier, M. R. Sestier, and M. Gavend, *C. R. Soc. Biol.*, **150**, 1412 (1956).

[19] K. DeVoe, *Amer. J. Obstet. Gynecol.*, **105**, 304 (1969); M. M. Wellhöner, *Arch. Expt. Pathol. Pharmakol.*, **236**, 167 (1959); M. P. Embrey and M. J. Yates, *J. Obstet. Gynecol. Brit. Common.*, **71**, 33 (1964).

[20] A. Muhlrad, M. Kovacs, and G. Megyi, *Biochim. Biophys. Acta*, **107**, 507 (1965).

protected with a straight bore stopcock were spun at 1000 rpm in an International centrifuge (Model No. 50 size 1). Closed nmr samples containing precipitate were centrifuged upside down. Multifit hypodermic syringes (0.25–50 ml) equipped with 6–12-in. 18 gauge needles and one-way or two-way stopcocks (Becton and Dickenson) were used.

Acidimetric titration was carried out using Methyl Red as indicator.

Dineopentylmercury. Tetrahydrofuran in 250 ml of a solution containing 0.25 mol of neopentylmagnesium chloride was refluxed slowly into the condenser of a Soxhlet extractor charged with mercuric chloride (20 g, 0.074 mol). After 48 hr the reaction mixture was worked up by extraction into ether, and washing the ether layer with 10% aqueous sodium hydroxide and then distilled water. After drying the ether layer and removing solvent the dineopentylmercury was vacuum distilled through a small column at 70° (1 mm); yield 42 g, 64% (lit.[21,22] 67–69° (3 mm); yield 28% (in Et_2O)).

Dineopentylmagnesium. A thoroughly dry 250-ml side-arm flask was charged in the drybox with dineopentylmercury (17 g, 0.05 mol), powder grade 4 magnesium (Elektron magnesium) (2.1 g, 0.085 mol), and 50 ml of THF. This flask was fitted with a reflux condenser (operation under argon) and the contents refluxed for 12 hr; 1 ml of dineopentylmagnesium was added twice within 24 hr, and periodic titrations indicated the extent of conversion of R_2Hg to R_2Mg. The yield was 80%. Also several nmr spectra were obtained to monitor the progress of reaction.

The reaction vessel (minus condenser) was brought into the drybox and its contents syringed into a vacuum vial. The solution was dark brown with suspended magnesium in it. The vial was centrifuged twice to remove the suspension. Using the house vacuum line (15 mm), the contents of the vial was reduced to about 12 ml. After 3 hr long cylindrical crystals of dineopentylmagnesium had formed. The supernatant was removed, 5 ml of THF was added, and the purification was continued until the dineopentylmagnesium solution became colorless. The nmr spectrum is shown in Figure 7.

Isolation of Sparteine. Sparteine sulfate (20 g), Pfaltz and Bauer (0.06 mol), was mixed with 100 ml of 10% sodium hydroxide, in a 250-ml erlenmeyer flask. The aqueous layer was extracted five times with 50-ml portions of ether. The combined extracts were dried over $MgSO_4$, the ether was removed, and the sparteine was vacuum distilled at 130–132° (1 mm) (lit.[23] 134.5° (3 mm)).

Nmr, Preparation of Samples. For samples which were used for monitoring or evaluating reactions or for relatively low precision analytical work, a supply of nmr tubes was prepared in the laboratory using 5-mm glass ground to 0.195 ± 0.0005 in. o.d. by the Yorde Machine Company, Nelsonville, Ohio, open at both ends. They were cleaned with acetone, trisodium phosphate, aqua regia, ammonia, and distilled water and baked in an oven. The tubes were fitted with rubber serum caps and flamed under a stream of argon gas before use. They were filled in the drybox, if necessary, by oven-baked syringes and sealed off by flame while the contents were frozen in liquid nitrogen. For high precision kinetic studies, Wilmad (Imperial 5C7) nmr tubes were used. After rinsing once with acetone and distilled water and drying in the oven, the tube was connected *via* 5-mm glass tubing to a straight bore stopcock equipped with a 12/30 joint. This assembly was attached to the vacuum line and evacuated before use. The sample was syringed into the nmr tube in the drybox to a height 2–3 cm from the bottom. The sample was attached to the vacuum line and degassed by the conventional freeze–thaw cycle, usually repeated three or four times and then sealed off.

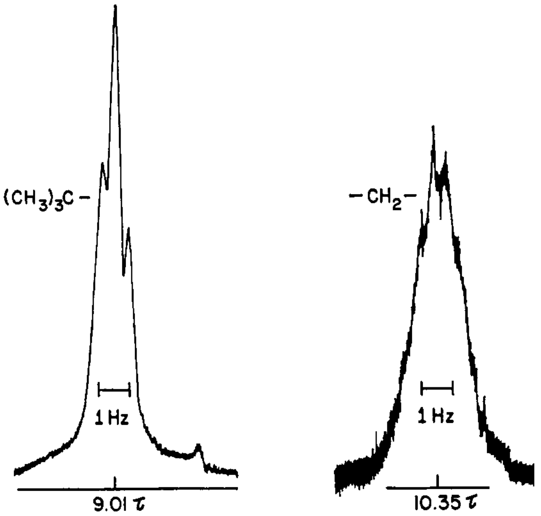


Figure 7. Nmr, 100 MHz, absorption for dineopentylmagnesium.

Nmr Spectra. Most of the preliminary spectra on product analysis were obtained with a Varian A-60-A variable-temperature nmr spectrometer.

The nmr spectra used for kinetic and equilibrium studies were determined with a Varian Model HA-100 spectrometer with the usual fixed-frequency internal lock reference system and variable temperature probe. In addition the spectrometer was equipped with a dc driven Wavetek audiofrequency sweep generator, which permits a wide selection of frequencies and sweep widths. The insert temperature was calibrated using the known temperature dependence of the CH_3 *vs.* OH chemical shift of methanol up to 50° and of ethylene glycol above 50°. For each temperature point the system was allowed to equilibrate 15 min for high temperature and 30 min for low temperature work. The chemical shift of the appropriate temperature standard was measured before and after the analytical spectra were obtained, and only those points were used which showed a temperature change of less than 2°. The reliability of the temperature was thus set at ±1°. In studies below 0°, care was taken to use only dry nitrogen since otherwise water condensed in the probe.

The spectra were all obtained using the frequency-sweep mode with an internal standard, usually a solvent peak, used as a reference. The field homogeneity was checked by measuring the per cent splitting of the outer doublet of *o*-dichlorobenzene. A resolution of 70% splitting (about 0.3 Hz line width) was the minimum acceptable for recording spectra.

Using the Wavetek sweep oscillator, the sweep width was adjusted so that the region of interest was just within the swept region, thus optimizing the widths and areas of the peaks. Each region was scanned from three to eight times depending on the size of the peaks and the reproducibility of the spectra. Spectra were scanned in both directions at a rate approximately 0.1 Hz/sec so as to minimize errors due to pen response time, satisfy slow passage conditions and still avoid saturation. The exact chemical shift of each line could be determined by counting the difference from the reference frequency to two points in the spectrum and interpolating points in between. Integration was accomplished by use of a K and E Compensating Polar Planimeter.

Acknowledgment. This research was supported by the National Science Foundation Grants No. GP 16402 and No. GP 36633X 1. The nmr equipment used was purchased in part with funds from a grant for permanent equipment from the National Science Foundation.

---

(21) F. C. Whitmore and E. Rohrmann, *J. Amer. Chem. Soc.*, **61**, 1591 (1939).

(22) Further details may be obtained by application to the authors.

(23) N. J. Leonard and R. E. Begler, *J. Amer. Chem. Soc.*, **72**, 1316 (1950).