Reactions of Dialkylmagnesium–Organolithium Solutions with Pyridine, Quinoline, and Cyclohexenone[1]

Herman G. Richey, Jr.,* and Julius Farkas, Jr.

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

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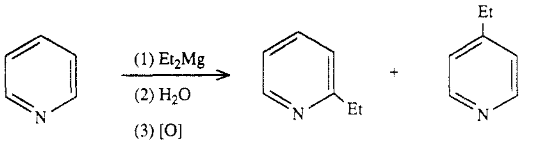
Reactions of pyridine with solutions prepared by mixing diethylmagnesium and ethyllithium solutions yield both 4-ethylpyridine and 2-ethylpyridine. By contrast, reactions of pyridine with either organometallic compound alone yield only 2-ethylpyridine. Reactions of 2-cyclohexen-1-one with the diethylmagnesium–ethyllithium solutions give considerably more of the 1,4-addition product (3-ethylcyclohexanone) than do reactions with either organometallic compound alone. Magnesiate species are thought to be responsible for the reactions, whose product compositions are similar to those obtained from reactions of solutions formed by addition of crown ethers or cryptands to dialkylmagnesium solutions.

A few years ago we noted some unusual reactions and reactivities of dialkylmagnesium solutions to which 15-crown-5 had been added. One unusual reaction was with pyridine and some substituted pyridines. Et_2Mg and pyridine react slowly to produce **1** (eq 1), a product resulting from 1,2-addition. Addition of the crown ether to solutions of Et_2Mg markedly accelerated the reaction with pyridine and led to formation of significant amounts of **2**, a product resulting from 1,4-addition.[2] On the basis of indirect evidence, we proposed that small amounts of magnesiate ions, formed by equilibria such as those illustrated in eq 2 and 3, might be responsible for the different behavior.[2]



(1)

1 **2**

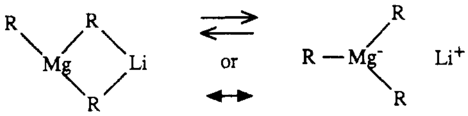
$$3R_2Mg + crown \rightleftharpoons Mg(crown)^{2+} + 2R_3Mg^- \quad (2)$$

$$3R_2Mg + crown \rightleftharpoons RMg(crown)^+ + R_5Mg_2^- \quad (3)$$

As one test of the proposal that magnesiate ions were present in the R_2Mg–crown ether solutions, we decided to prepare other solutions that might reasonably contain magnesiate ions or closely related species and to compare behavior in some reactions of these solutions and the R_2Mg–crown ether solutions.

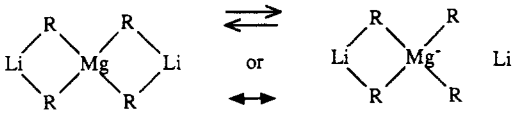
Solutions prepared by mixing dialkylmagnesium and organolithium compounds seemed to be a particularly good choice for study. Wittig et al. reported that phenyllithium and diphenylmagnesium in diethyl ether produce a solid of composition $MgLiPh_3$,[3] and Coates and Heslop observed that butyllithium and dimethylmagnesium in diethyl ether furnish a viscous liquid of composition $MgLiMe_2Bu(Et_2O)$.[4] Thorough NMR investigations by Brown, Seitz, and Little of solutions prepared by mixing diorganomagnesium and organolithium compounds in various ratios established the formation of rapidly equilibrating, mixed-metal compounds of at least three stoichiometries (**3**–**5**).[5–7] The composition of a particular solution depends on the nature of R and the solvent. Dimethylmagnesium and methyllithium in diethyl ether, for example, produce **4** and **5** but not **3**.[5] It is believed that these mixed-metal compounds have structures with bridging alkyl groups: for example, structure **6** for R_3MgLi (**3**) and structure **8** for R_4MgLi_2 (**4**), with sufficient ether molecules also bonded to the metal atoms to make each at least tetracoordinate. More recently, single-crystal X-ray diffraction studies have shown **8** to be the structure of two solids (R = Me or Ph), in which each lithium also is bonded to both nitrogens of a tetramethylethylenediamine (TMEDA).[8]

$$R_2Mg + RLi \rightarrow \underset{\mathbf{3}}{R_3MgLi} + \underset{\mathbf{4}}{R_4MgLi_2} + \underset{\mathbf{5}}{R_5MgLi_3} \quad (4)$$



(5)

6 **7**



(6)

8 **9**

It is reasonable that such mixed-metal species could have significant anionic character at magnesium. Structures **7** and **9** could be canonical structures of resonance hybrids describing the bonding, or ionization to discrete ions (**6** → **7** and **8** → **9**) might even be significant. Therefore we set out to determine if solutions prepared from Et_2Mg and EtLi would have reaction behavior similar to that exhibited

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[1] Most of this work is taken from Farkas, J. Ph.D. Dissertation, The Pennsylvania State University, 1985. Some preliminary results appeared in: Richey, H. G., Jr.; Farkas, J., Jr. *Tetrahedron Lett.* **1985**, 275.

[2] Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672.

[3] Wittig, G.; Meyer, F. J.; Lange, G. *Liebigs Ann. Chem.* **1951**, *571*, 167.

[4] Coates, G. E.; Heslop, J. A. *J. Chem. Soc. A* **1968**, 514.

[5] Seitz, L. M.; Brown, T. L. *J. Am. Chem. Soc.* **1966**, *88*, 4140.

[6] Seitz, L. M.; Brown, T. L. *J. Am. Chem. Soc.* **1967**, *89*, 1602. Seitz, L. M.; Little, B. F. *J. Organomet. Chem.* **1969**, *18*, 227. Also see: House, H. O.; Lantham, R. A.; Whitesides, G. M. *J. Org. Chem.* **1967**, *32*, 2481.

[7] The organolithium compounds of course are themselves oligomers [for a review see: Wardell, J. L. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, 1982; Chapter 2] as to a lesser extent are the organomagnesium compounds [for a review see: Lindsell, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, 1982; Chapter 4].

[8] Thoennes, D.; Weiss, E. *Chem. Ber.* **1978**, *111*, 3726. Grieser, T.; Kopf, J.; Thoennes, D.; Weiss, E. *Chem. Ber.* **1981**, *114*, 209. For a related structure, $Li(TMEDA)_2{}^+Bzl_2MgBzl_2Li(TMEDA)^-$, see: Schubert, B.; Weiss, E. *Chem. Ber.* **1984**, *117*, 366.

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Table I. Product Compositions from Reactions of Organometallic Compounds and Pyridine in Diethyl Ether[a] at 25 °C

rel molar amts								
Et_2Mg	EtLi	pyridine	additive	additive	time, h	[pyridine], M	1,[b] %	2,[b] %
1	0	1	0		22	0.30	0.3	0
1	0	1	0.5	$Me_2NCH_2CH_2NMe_2$	22	0.27	0.3	0
1	0	1	1.5	12-crown-4	22	0.40	0.1	0
1	0	1	1	15-crown-5[c]	20	0.20	11	37
1	0	2	2	15-crown-5[d]	72	0.64	13	37
1	0	1	1	2,1,1-cryptand[e]	24	0.10	14	31
1	0	1	2	2,2,1-cryptand[e]	24	0.10	15	10
0	1	1	0		0.5	0.14	39	0
0	1	1	0		2	0.14	40	0
0	1	1	0		22	0.14	47	0
1	1	1	0		22	0.24	37 (31)	6 (7)
2	1	2	0		22	0.19	51 (43)	21 (20)
4	1	4	0		0.5	0.22	21	3
4	1	4	0		4	0.22	52	9
4	1	4	0		8	0.22	62	12
4	1	4	0		20	0.22	69 (63)	18 (14)
4	1	4	1.5	$Me_2NCH_2CH_2NMe_2$	22	0.25	73 (78)	23 (23)
4	1	4	1.5	$(Me_2N)_3P{=}O$	22	0.12	79	12
2	1	2	1.5	12-crown-4	22	0.25	24	13
4	1	4	1.5	12-crown-4	0.5	0.16	7	7
4	1	4	1.5	12-crown-4	4	0.16	15	24
4	1	4	1.5	12-crown-4	9	0.16	22	38
4	1	4	1.5	12-crown-4	22	0.16	26	46
4	1	4	1.5	12-crown-4	39	0.18	25	47
4	1	4	3.0	12-crown-4	22	0.12	27	54
4	1	4	1.5	15-crown-5	22	0.18	17	37
4	1	4	1.5	18-crown-6	22	0.18	18	42
4	1	4	1.5	2,1,1-cryptand	22	0.18	44	38

[a] Since a benzene solution of EtLi was used, some benzene also was present in the Et_2Mg–EtLi solutions, but never more than 25% of the volume. [b] Yields are based on EtLi if it is present and on Et_2Mg (assuming that only one Et will react) when EtLi is not present. Yields in parentheses are from duplicate experiments. The products could be detected reliably down to a level of about 0.1%. In diethyl ether at 40 °C. King, B. A. Ph.D. Dissertation, The Pennsylvania State University, 1984. [d] In tetrahydrofuran at 40 °C.[2] [e] Reference 11.

by solutions of Et_2Mg and a crown ether.

There are some prior reports of reactions of diorganomagnesium–organolithium solutions. One study was of reactions of Ph_2Mg–PhLi solutions with a hydrocarbon, fluorene, and with ketones, benzophenone, and benzalacetophenone.[3] With benzalacetophenone, PhLi alone gave principally a product of 1,2-addition, but either Ph_2Mg alone or the mixture gave primarily a product of 1,4-addition. All gave the same products with fluorene and benzophenone. Another study concerned the stereochemistry (cis or trans) of the products formed on addition to several cyclic ketones.[9] Me_2Mg alone, MeLi alone, and a mixture of the two formed similar product mixtures. Mixtures of organomagnesium compounds and organolithium compounds have also been used as catalysts for diene and styrene polymerizations.[10]

After this work had begun, we demonstrated convincingly that magnesiate ions are formed from R_2Mg by addition of cryptands that coordinate more efficiently to Mg than does 15-crown-5.[11-13] For example, ^1H NMR observations suggested essentially quantitative formation in solutions of Np_3Mg^- (Np = neopentyl) and Et_3Mg^- (or oligomers of these ions) and single-crystal X-ray diffraction studies demonstrated two solids to be $NpMg(2,1,1\text{-cryptand})^+Np_3Mg^-$ and $[EtMg(2,2,1\text{-cryptand})^+]_2Et_6Mg_2^{2-}$.[11] More recently, we have found that in the noncoordinating solvent benzene, even 15-crown-5 can form significant amounts of $RMg(crown)^+$ ions.[13,14] The counterions must be magnesiate ions, although since exchange is rapid on the NMR time scale, only single absorptions are seen for all R groups of magnesiate ions and neutral species. In fact, a single-crystal X-ray diffraction study demonstrated a solid to consist of $MeMg(15\text{-crown-}5)^+$ cations and polymeric $[Me_5Mg_2^-]_n$ anions.[14] These more recent studies now render far more likely the proposal that magnesiate ions form in small amounts from R_2Mg and 15-crown-5 in diethyl ether. Nevertheless, the study reported here concerning solutions prepared from R_2Mg and RLi has furnished interesting results. Moreover, we would not have anticipated these results if we had not suspected that, due to formation of magnesiate species, the behavior of R_2Mg–RLi and R_2Mg–crown ether solutions might be similar.

Results

Reactions with Pyridine. Representative reactions with pyridine are summarized in Table I. Besides recovered pyridine, **1** and **2** generally were the only compounds detected in significant amounts in any of the reactions. The reactions initially must lead to **10** and **11** (Scheme I; when Et_2Mg–EtLi solutions are used, the metal in **10** and **11** also can be Li, of course).[15] Hydrolysis then would furnish dihydropyridines **12** and **13**, which would be readily oxidized to **1** and **2**.[16] In fact, gas chromato-

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(9) Ashby, E. C.; Chao, L.-C.; Laemmle, J. *J. Org. Chem.* **1974**, *39*, 3258.

(10) See for example: Hsieh, H. L.; Wang, I. W. *Macromolecules* **1986**, *19*, 299, and references therein.

(11) Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 432.

(12) Richey, H. G., Jr.; Kushlan, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 2510.

(13) Kushlan, D. M.; Pajerski, A. D. The Pennsylvania State University, unpublished results.

(14) Pajerski, A. D.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2660.

(15) Elimination of LiH from compounds such as **10** and **11** generally requires heating at temperatures considerably above the reaction temperature used in this work [for example, ref 16 and Foster, R.; Fyfe, C. A. *Tetrahedron* **1969**, *25*, 1489].

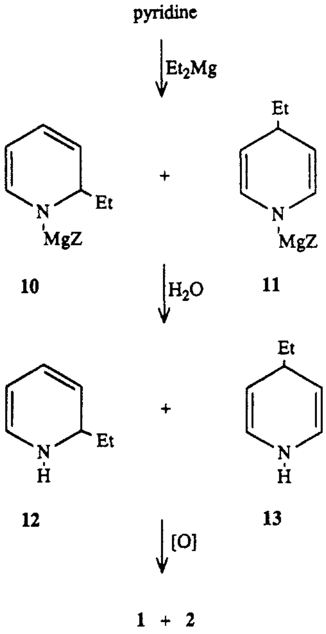
(16) Oxidation of dihydropyridines, even by air, is known to be ready [refs 17 and 18, and Scriven, E. F. V. In *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 2, Chapter 5].

Table II. Product Compositions from Reactions of Organometallic Compounds and Quinoline in Diethyl Ether[a] at 25 °C

rel molar amts[b]								
Et_2Mg	EtLi	quinoline	additive	additive	time, h	quinoline,[c] %	14 + 15,[c] %	16 + 17,[c] %
4	0	1	0		0.25	95	4	0
4	0	1	0		2	80	17	0
4	0	1	0		4	58	28	0
4	0	1	0		9	31	56	0
4	0	1	0		24	14	86	0
4	0	1	4	15-crown-5	0.25	1	68	15[d]
0	2	1	0		1	0	95	0
4	1	1	0		1	0	96	0
4	1	1	1.5	12-crown-4	1	0	88	6[e]

[a] Since a benzene solution of EtLi was used, some benzene also was present in the Et_2Mg–EtLi solutions, but never more than 10% of the volume. [b] The concentration of quinoline was ~0.1 M. [c] Yields are based on quinoline. [d] A mixture containing 40% of 16 and 60% of 17. [e] Mainly 17.

Scheme I



graphic analysis of the product mixtures occasionally have shown additional products, whose mass spectra are reasonable for dihydropyridines. These additional products disappear following additional exposure to air.

As shown by the first entry, Et_2Mg and pyridine react only slowly to produce exclusively 1. It was shown that not even a 0.01% yield of 2 was present.[2] This addition is not accelerated by TMEDA or 12-crown-4. Addition of 15-crown-5, 2,1,1-cryptand, or 2,2,1-cryptand, however, leads to reactions that are more rapid and that produce significant amounts of 2, as well as of 1. EtLi alone, of course, reacts rapidly with pyridine to produce only 1.[19] No products resulting from addition are noted when 12-crown-4 also is present, apparently because of rapid destruction of the EtLi by reaction with 12-crown-4.[21]

It is then striking that solutions prepared from Et_2Mg plus EtLi produce product mixtures containing significant amounts of 2, *a product not formed in reactions of pyridine and either organometallic compound alone.* The remarkable reaction of pyridine with Et_2Mg–crown ether or Et_2Mg–cryptand solutions therefore also takes place with Et_2Mg–EtLi solutions. The ratio of 2 to 1 varies somewhat with the Et_2Mg:EtLi:pyridine ratios. Data for several reactions differing only in reaction time indicate that less than one-half of the ultimate amounts of 1 and 2 have formed after 0.5 h. The qualitative results (considerable product formed after only 0.5 h but some product still forming after 8 h) indicate a complicated kinetic behavior, probably due at least in part to shifting compositions of the organometallic reactants. Nevertheless, a reaction with Et_2Mg–EtLi clearly is far more rapid than with Et_2Mg alone, though probably not as rapid as with primary organolithium compounds[22] alone. With Et_2Zn in place of Et_2Mg (Et_2Zn:EtLi was 4) in the presence or absence of 12-crown-4, neither 1 nor 2 was formed and substantial amounts of pyridine were recovered. Et_2Zn alone did not react significantly with pyridine, of course.

The presence of 12-crown-4 in the Et_2Mg–EtLi solutions possibly decreases slightly the rate of reaction with pyridine but does increase significantly the 2:1 product ratio. This ratio also is increased by 15-crown-5, 18-crown-6, or 2,1,1-cryptand but not by TMEDA or hexamethylphosphoramide. Of these additives, only 15-crown-5 and 2,1,1-cryptand lead to formation of 2 in reactions of pyridine and Et_2Mg alone. Addition of 12-crown-4 or 2,1,1-cryptand leads to appearance of a second liquid phase (^1H NMR spectra indicate that most ethyl groups bonded to a metal and most crown ether or cryptand residues are in the lower phase); the reactions with these systems were done with the mixture of phases. In contrast to the rapid destruction of 12-crown-4 by EtLi, a mixture prepared from Et_2Mg, EtLi, and 12-crown-4 (4:1:1.5) showed significant ^1H NMR absorptions for the crown ether and for ethyl groups attached to a metal, even after 25 h.

Ratios of 2:1 were similar for reactions run for different times. Note, for example, a series of reactions having Et_2Mg:EtLi:pyridine ratios of 4:1:4 (0.5–20 h) and a similar series in which 12-crown-4 also was present. Therefore, there is not a slow equilibration that alters the product composition.

Reactions with Quinolines. Reactions with quinoline are summarized in Table II. Reactions with Et_2Mg furnish, besides recovered quinoline, only 14 and 15 (Scheme II), products with ethyl groups attached to C-2. These products were clearly identified by their ^1H NMR spectra. Moreover, upon exposure of a diethyl ether solution containing both products to air at ambient temperature, the GC peak due to 15 gradually diminishes with a concomitant increase in the intensity of the peak due to 14. This

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(17) Fraenkel, G.; Cooper, J. C. *Tetrahedron Lett.* **1968**, 1825.

(18) Fowler, F. W. In *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 2, Chapter 7.

(19) Only 1,2-addition products are formed from RLi and pyridine.[20]

(20) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: Oxford, 1974; Chapter 8.

(21) A ^1H NMR spectrum of a solution prepared by addition of 12-crown-4 to the EtLi solution was devoid of absorptions that could be attributed to ethyl groups bound to lithium.

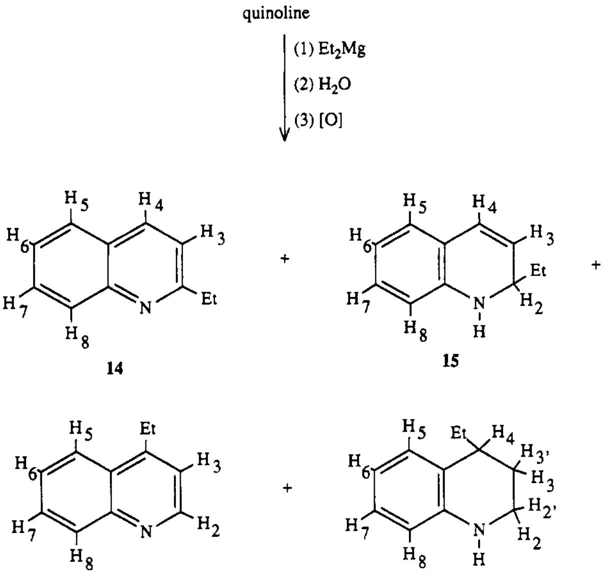
(22) For example, compare with the rapid addition to pyridine of butyllithium.[17]

Table III. Product Compositions from Reactions of Organometallic Compounds and 2-Cyclohexen-1-one in Diethyl Ether[a] at 25 °C

rel molar amts							
Et$_2$Mg	EtLi	cyclohexenone	additive	additive	18,[b] %	19,[b] %	20,[b] %
4	0	1	0		67	2	0
2	0	1	2	15-crown-5[c]	57	34	0
1	0	0.5	1	2,1,1-cryptand[d]	25	18	0
1	0	0.5	2	2,1,1-cryptand[d]	40	30	0
0	1	1	0		73	0	0
4	1	1	0		60	7	6
4	1	1	1.5	12-crown-4	58	11	3
0	2	1	1	CuI[e]	0	91	0

[a] Since a benzene solution of EtLi was used, some benzene also was present in the Et$_2$Mg–EtLi solutions, but never more than 10% of the volume. [b] Yields are based on cyclohexenone. [c] King, B. A. Ph.D. Dissertation, The Pennsylvania State University, 1981. [d] Squiller, E. P. Ph.D. Dissertation, The Pennsylvania State University, 1984. [e] This corresponds to "Et$_2$CuLi". The temperature was −15 °C; the product composition from a reaction at −60 °C was the same.

Scheme II



14 15 16 17

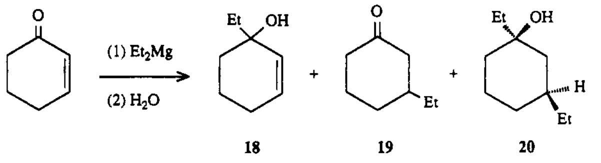
oxidation can be accelerated by refluxing the solution with FeCl$_3$.[23] Since dihydropyridines are oxidized more readily than dihydroquinolines, observation of a dihydroquinoline increases the likelihood that dihydropyridines are formed in the similar reactions with pyridine.

Reactions of Et$_2$Mg are considerably more rapid when 15-crown-5 is added and, besides 14 and 15, produce small amounts of two additional products. The ^{1}H NMR spectrum of one clearly identifies it as 17.[24] The ^{1}H NMR spectrum of the second is consistent with the assignment of structure 16.[25] Moreover, formation together of a quinoline (16) and related tetrahydroquinoline (17) also is consistent with structure 16. Both 16 and 17 could form by disproportionation of 4-ethyl-1,4-dihydroquinoline, the probable initial product. Such disproportionations of dihydroquinolines to quinolines and tetrahydroquinolines are known.[18] Compounds 16 and 17 were not present in significant amounts in reactions with Et$_2$Mg–EtLi solutions, although some 16 was obtained from such a reaction in which 12-crown-4 also was present.

A crown ether increases the rate of reaction of Et$_2$Mg with quinoline, as with pyridine. The ratio of 4-ethyl to 2-ethyl products formed upon addition to Et$_2$Mg of a crown ether or EtLi, however, is less in reactions with quinoline than with pyridine.

Reactions with 2-Alkylquinolines. In an effort to increase the amount of 1,4-addition, some reactions were carried out (23 h) with 2-alkylquinolines. Reactions of 2-methylquinoline with Et$_2$Mg alone and with added 15-crown-5 or EtLi furnished only recovered reactant, as did reactions of 2-ethylquinoline with Et$_2$Mg alone and with added 15-crown-5. GC-MS analysis of the reactant recovered from a reaction of 2-methylquinoline and Et$_2$Mg that was hydrolyzed with D$_2$O showed the majority of the molecules to be monodeuterated. Presumably metalation of the methyl group had taken place.

Reactions with Cyclohexenone. Organomagnesium compounds add to most α,β-unsaturated aldehydes and ketones to give principally the products of 1,2-addition. As shown by the first entry of Table III, Et$_2$Mg added to 2-cyclohexen-1-one to produce mainly 18 (eq 7) and only small amounts of the 1,4-addition product, 19. As indicated by the sampling of data in Table III, crown ethers and cryptands increase significantly the amount of 19. Organolithium compounds are even more prone than organomagnesium compounds to give 1,2-addition products,[26] and, as indicated in an entry in Table III, a reaction of EtLi and cyclohexenone did not produce a detectable amount (>0.5%) of 19. Solutions prepared from Et$_2$Mg and EtLi, however, gave more 19 than did Et$_2$Mg alone, and the amount was even larger if 12-crown-4 also was present.



(7)

18 19 20

The reactions with Et$_2$Mg–EtLi solutions also produced small amounts of a dialkylated product that was found to be *trans*-1,3-diethyl-1-cyclohexanol (20). It was evident from the ^{1}H NMR and mass spectra of this compound that it is a 1-ethyl-1-cyclohexanol with an additional ethyl group. Either C-2 or C-3 are possible sites for attachment of the second ethyl group. The assignment of structure 20 (see Experimental Section) was made primarily because the ^{1}H NMR spectrum was essentially identical with that

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(23) FeCl$_3$ was shown to be effective in an oxidation of 4-methyl-1,2-dihydroquinoline to 4-methylquinoline [Ogata, Y.; Kawasaki, A.; Suyama, S. *Tetrahedron* **1969**, *25*, 1361].

(24) The ^{1}H NMR spectrum is very similar to that reported for a CCl$_4$ solution of this compound [Noyori, R.; Katô, M.; Kawanisi, M.; Nozaki, H. *Tetrahedron* **1969**, *25*, 1125].

(25) This compound has been reported many times, but we could not find a full description of its ^{1}H NMR spectrum. Because of problems detailed in the Experimental Section, the quality of the spectrum was mediocre, and the spectrum alone might not rigorously exclude the possibility that the Et substituent is attached to a carbon in the carbocyclic ring. By analogy with the products of reactions with pyridine, however, structure 16 certainly is most likely.

(26) Reference 20, Chapter 9.

of an authentic sample of 1,3-diethyl-1-cyclohexanol in which the trans isomer (**20**) predominated.[27,28]

Discussion

Reactions of pyridine with solutions prepared from Et_2Mg and EtLi lead to formation of significant amounts of **2**, a product not noted in reactions with either organometallic alone. Since product **1** can form with EtLi alone, however, it is not possible from the product mixtures formed with Et_2Mg–EtLi solutions to conclude what 2:1 ratio is characteristic of reactions of magnesiate ions. In the reactions involving R_2Mg and added cryptands or crown ethers, however, it is likely that magnesiate ions are responsible for the formation not only of **2** but also of **1**, since little **1** forms in the absence of the additives. We think it likely that the mechanism of reaction of magnesiate species with pyridine is one that forms both **1** and **2**, the balance between these products being sensitive to minor changes in the reactant, for example, in the nature of the counterion or the state of aggregation.

One mechanistic possibility is a process that leads to formation of a pyridine radical anion, to which an ethyl group becomes attached either at C-2 or C-4 in a subsequent product-determining step. Electron transfer already is implicated as a key mechanistic step in some reactions of conventional organomagnesium compounds,[29] and a magnesiate ion should be a more potent electron-transfer reagent than the corresponding neutral organomagnesium compound. Significant formation of 4-alkylpyridines rather than of 2-alkylpyridines also is observed in reactions of an alkyl halide, magnesium, and pyridine that were studied by Bryce-Smith, Morris, and Wakefield.[30] The pyridine radical anion was suggested to be an intermediate in these reactions. Large amounts of 4-alkylpyridines also are formed in reactions of pyridine with allylmagnesium bromide[31] or benzylmagnesium compounds.[32] Because of the stability of the alkyl radicals that might result, electron-transfer mechanisms could be unusually favorable with allyl and benzyl organomagnesium compounds.

With cyclohexenone, Et_2Mg–EtLi solutions gave more product of 1,4-addition (**19**) than did an Et_2Mg solution. Since **18** forms significantly from either Et_2Mg or EtLi alone, however, it is uncertain just what ratio of **19** to **18** is characteristic of reactions of magnesiate species. Particularly since the amount of **18** is significant in the reactions even with Et_2Mg and cryptands, however, we think it likely that reactions of magnesiate ions produce some **18**. This behavior differs somewhat from that of zincates and markedly from that of cuprates. Zincate species (e.g., R_3ZnLi) have been observed to react with some α,β-unsaturated ketones, including cyclohexenone, to give mainly, and in some instances exclusively, products of 1,4-addition.[33] In reactions with α,β-unsaturated ketones, cuprates can lead virtually completely to 1,4-addition products.[34] As indicated by an entry in Table III, a solution of "Et_2CuLi" gave **19** as the only product.

Interpretation of the increased 2:1 ratio in reactions with pyridine when crown ethers or cryptands are added to Et_2Mg–EtLi solutions is complicated by the fact that **1** (but not **2**) can arise from a reaction of EtLi in the absence of Et_2Mg or of Et_2Mg plus a coordinating agent. One effect of a coordinating agent could be to reduce the amount of EtLi not incorporated into mixed Et_2Mg–EtLi species and hence decrease the portion of the product formed by reaction with EtLi rather than with mixed species. Another effect of an additive could be, by coordination with Li^+, to enhance ionizations such as **6** → **7** and **8** → **9** (or enhance the contribution of the ionic canonical forms in **6** ↔ **7** and **8** ↔ **9**), as a consequence changing the product ratio.

This work demonstrates that solutions prepared by mixing solutions of dialkylmagnesium and alkyllithium compounds exhibit behavior different from that of either organometallic compound alone. Moreover, this behavior is similar to that observed when crown ethers or cryptands are added to dialkylmagnesium compounds. It is reasonable to attribute this behavior to magnesiate species.

Experimental Section

^1H NMR spectra were taken at 360 MHz; chemical shifts are reported in ppm (δ) downfield from internal Me_4Si. Absorptions are reported using the following notations: s, singlet; d, doublet; t, triplet; q, quartet; m, a more complex multiplet; c, complex overlapping absorptions; br, broad. Analytical GC separations were performed with instruments with flame ionization detectors, helium as the carrier gas, and the following columns: A, SE-30 (20%) on Gas Chrom Q (100–120 mesh), 2 mm i.d. × 10 ft (glass); B, SP2401 (5%) on Supelcoport (100–120 mesh), 2 mm i.d. × 6 ft (stainless steel); C, SPB-1 bonded coating (1.5 μm thick), 0.53 mm i.d. × 15 m (quartz). The instruments were interfaced with electronic integrators. The amounts of components of reaction mixtures were determined by the areas of their GC peaks relative to that of the peak due to an internal standard. The values determined or assumed for response factors are indicated with the procedures for reactions of each substrate. Preparative GC separations were performed with an instrument with a thermal conductivity detector and the following column: SE-30 (20%) on Gas Chrom Q (80–100 mesh), 0.25 in. o.d. × 10 ft (aluminum). Small samples were collected for spectral analysis by using glass U-shaped tubes cooled in liquid nitrogen and inserted into the exit port of the chromatograph. GC-MS analyses were performed with a Finnigan 9500 gas chromatograph and a Finnigan 3200 mass spectrometer. Air-sensitive materials were handled in a glovebox under an atmosphere of purified, dry nitrogen. All glassware was oven-dried (135 °C) prior to use.

Materials. EtBr and 2-cyclohexen-1-one were dried over $CaCl_2$ and then distilled before use. Benzene, dioxane, hexamethylphosphoramide, pyridine, and tetramethylethylenediamine (TMEDA) were distilled from CaH_2 and stored over molecular sieves (4 A). Quinoline and quinaldine were distilled and stored over molecular sieves (4 A). Diethyl ether was distilled from sodium benzophenone ketyl prior to use. 12-Crown-4, 15-crown-5,

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(27) Organolithium compounds [for a review see: Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 1] and some favorable organomagnesium compounds [for a review see: Vara Prasad, J. V. N.; Pillai, C. N. *J. Organomet. Chem.* **1983**, *259*, 1] are known to add to the carbon–carbon bonds of some metalated unsaturated alcohols. Attachment of the second ethyl group at C-2 would presumably have proceeded by addition to metalated **18** and would be expected to give *trans*-1,2-diethyl-1-cyclohexanol (hydroxyl and 2-ethyl cis). The spectrum of the product, however, was quite different from that of an authentic sample of this isomer.

(28) Since **20** was such a minor product, its origin was not further investigated. It is unlikely, however, that it formed by addition to metalated **18**. Attachment of the organic group to C-3 of 2-alken-1-ols places the metal and O on adjoining carbons and, particularly in reactions with cycloalkenols, results in elimination of these groups to form an alkene [see for example: Crandall, J. K.; Clark, A. C. *J. Org. Chem.* **1972**, *26*, 4236. Eisch, J. J.; Merkley, J. H.; Galle, J. E. *J. Org. Chem.* **1979**, *44*, 587]. It is more likely that **20** was formed by an addition to **19**; one possibility is by addition of remaining organometallic to **19** just as this ketone is being formed from its enolate during quenching with water.

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18-crown-6, and 2-ethyl-1-cyclohexanol were commercial samples (Aldrich Chemical Co.) as were 2,1,1-cryptand and 2,2,1-cryptand (MCB Chemicals, Inc.) and Et_2Hg (Morton Thiokol, Inc., Alfa Products); all were used without further purification. Lithium was obtained as a 30% dispersion in mineral oil (Morton Thiokol, Inc., Alfa Products) and Mg as small pieces (Cerac, Inc., 99.99%).

1,2- and 1,3-Diethyl-1-cyclohexanols. 2-Ethylcyclohexanone was synthesized by oxidation[35] of a sample of *cis*- and *trans*-2-ethyl-1-cyclohexanols.[36] A reaction[37] of that ketone and EtMgBr produced a mixture of *cis*- and *trans*-1,2-diethyl-1-cyclohexanols: bp 79 °C (4 Torr) [lit.[37] bp 72–73 °C (3 Torr)]; ^1H NMR ($CDCl_3$) δ 0.95–1.75 (c), 0.89 (t, $J = 7.5$ Hz, CH_3), 0.85 (t, $J = 7.5$ Hz, CH_3). GC analysis (column C, 60 °C for 3 min, then programmed at 10 °C/min to a final temperature of 200 °C) showed two significant peaks (11.68 and 11.84 min) in the 12:1 ratio already reported[38] for this mixture, the trans isomer being the principal isomer. The mass spectra of both peaks were similar: m/z (rel intensity) 156 (M^+, not seen), 138 (25), 109 (100), 81 (25).

3-Ethylcyclohexanone (**19**) was synthesized by CuI-catalyzed addition of EtMgBr to 2-cyclohexen-1-one following a procedure that has been used with similar compounds.[39] A standard reaction of **19** (which was somewhat contaminated with **18**) and EtMgBr in diethyl ether produced a mixture of 1,3-diethylcyclohexanols: bp 51–54 °C (0.15 Torr). GC analysis (column C, same conditions as in preceding paragraph) showed two significant peaks (11.27 and 11.42 min) in an approximately 4:1 ratio. Presumably these are, respectively, the trans (**20**) and cis isomers.[40] A sample for a ^1H NMR spectrum was purified further by preparative GC (which would not, however, have significantly separated the cis and trans isomers). The ^1H NMR spectrum ($CDCl_3$) is complex with many absorptions overlapping, but the following are reasonable assignments and areas for the major absorptions: 1.77 (br m though appears somewhat like a br d with $J = 11$ Hz, 1), 1.45–1.75 (c, 6), 1.46 (q, 2, $J = 7.5$ Hz, $OCCH_2$), ~1.25 (m, 1), 1.22 (appearance of quintet, 2, $J = 7.5$ Hz, $HCCH_2CH_3$), 1.12 (br s, ~1, OH?), 0.92 (t, 3, $J = 7.6$ Hz, CH_3), 0.89 (t, 3, $J = 7.4$ Hz, CH_3), 0.78 (bm, 1); mass spectrum (GC peaks for the two isomers not fully resolved), m/z (rel intensity) [mainly major isomer] 156 (M^+, not seen), 138 (20), 109 (100), 67 (45); [mainly minor isomer] 156 (M^+, not seen), 138 (25), 109 (100), 67 (65).

Et_2Mg. EtMgBr solutions (approximately 1.0 M) were prepared in a standard way from EtBr, Mg (1.33 equiv), and diethyl ether. The concentrations of the resulting solutions were determined by hydrolysis of an aliquot, addition of an excess of a standard HCl solution, and titration with a standard NaOH solution using bromothymol blue as the indicator. A solution of dioxane (0.15 mol) in diethyl ether (50 mL) was added dropwise to the EtMgBr solution (0.15 mol) over 2 h. The resulting slurry was stirred for an additional 15 h using a magnetic stirring bar. If the slurry was too viscous, additional ether was added until efficient stirring was achieved. The slurry then was centrifuged. Addition of small amounts of dioxane caused no further precipitation. The solution was titrated as before to determine total base concentration. Mg concentration was determined by hydrolysis of an aliquot, which then was adjusted to pH 10 by addition of a $NaOH–NaHCO_3$ buffer solution and titrated with a standard EDTA solution using eriochrome black T as the indicator (purple to blue color change). The Mg concentration was always within 5% of one-half of the base concentration. The concentration of Et_2Mg ordinarily was about 0.4 M.

EtLi.[41] The preparation was carried out in a 200-mL, round-bottomed flask to which was attached a side arm with a Teflon stopcock which was used for addition of reagents and a condenser to the top of which was attached a side arm connected to a source of purified nitrogen that maintained a positive pressure in the apparatus. The apparatus was flushed thoroughly with nitrogen, and a magnetic stirring bar and lithium dispersion in mineral oil (6.7 g, corresponding to 2.0 g, 0.29 mol, of Li) were added to the flask. Mineral oil was removed by repeatedly adding pentane (10-mL portions), allowing the contents to stir for several minutes, and then removing the pentane with a syringe. Benzene (45 mL) and then Et_2Hg (3.17 mL, 0.030 mol) were added and the flask was heated at 65 °C for 20 h. During this period cold methanol (−75 °C) was pumped through the condenser to condense Et_2Hg vapors. The solvent was removed under reduced pressure, and the residue heated at 40 °C under vacuum (0.01 Torr) for 5 h to remove any unreacted Et_2Hg. Benzene (50 mL) was added and the contents of the flask were stirred for 5 h and then filtered through a fritted funnel into a Schlenk flask. The base concentration was determined by the same titration procedure used for organomagnesium solutions. The concentration of EtLi was about 0.7 M.

Reactions with Pyridine. The solutions were prepared in a glovebox. The appropriate amount of EtLi solution was added with a syringe to a vial containing Et_2Mg solution (2 mmol) that was stirred with a magnetic stirring bar, resulting in all instances in homogeneous solutions. A diethyl ether solution (~0.5 M) of the appropriate coordinating agent was added and the contents of the vial were stirred for 5 min. Addition of 12-crown-4 or 2,1,1-cryptand to Et_2Mg–EtLi solutions resulted in the formation of a second liquid phase. Addition of 15-crown-5 or 18-crown-6 produced some turbidity but no evident second phase. HMPA and TMEDA produced no visual effects. A diethyl ether solution of pyridine (~0.5 M) containing a known amount of decane for use as a GC standard was added. Addition of pyridine to the Et_2Mg–EtLi solutions produced yellow solutions. Yellow solutions also were noted when 2,1,1-cryptand, TMEDA, or HMPA was present. The reactions containing 12-crown-4, 15-crown-5, or 18-crown-6 successively turned orange, red, and purple. The vial was removed from the glovebox and cooled in ice, and its contents were hydrolyzed by addition of a saturated NH_4Cl solution (5 mL). Aqueous sodium hydroxide (1 mL) was added to adjust the pH to about 10. The aqueous layer was extracted with two 5-mL portions of diethyl ether, which were combined and dried (Na_2SO_4). Typical retention times in the GC analyses (column A, 100 °C for 4 min, then programmed at 40 °C/min to a final temperature of 185 °C) were pyridine (4.4 min), **1** (6.8), **2** (7.6), and decane (8.0). Products were identified by comparison of retention times to those of authentic samples. Response factors relative to decane, determined by using standard solutions prepared from authentic samples, were 1.32 for pyridine, 1.20 for **1**, and 1.25 for **2**.

Reactions with Quinoline. The procedure for the reactions was similar to that used for the reactions with pyridine except that undecane was the internal standard. Typical retention times in the GC analyses (column B, 70 °C for 3 min, then programmed at 30 °C/min to a final temperature of 130 °C) were undecane (3.4 min), quinoline (6.8), **14** (7.8), **17** (9.5), **15** (10.2), and **16** (11.3). The response factor of quinoline relative to undecane was determined to be 1.20. The response factors of **14**–**17** were assumed also to be 1.20. Because the peaks were relatively close together, it was not possible to collect samples of some of the products that were not contaminated somewhat with other products. To eliminate contamination by **15** in the samples of **16** and **17**, before GC collections were begun the reaction products containing these compounds were allowed to stand in air until all **15** had been oxidized to **14**. All samples were somewhat contaminated with the major product, **14**; this problem was most troublesome in the sample of material thought to be **16**, particularly since some features of the spectra of **14** and **16** are very similar. The ^1H NMR spectra ($CDCl_3$) and tentative assignments of the absorptions are as follows:

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[40] For a review of stereochemistries of additions of Grignard reagents to cycloalkanones, see: Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521.

[41] The procedure is adapted from the following and references cited therein: Schöllkopf, U. *Methoden Org. Chem. (Houben-Weyl), 4th ed.* **1970**, *13* (part 1), 128.

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14: δ 8.07 and 8.04 (overlapping d's, 2, H_8 and H_4), 7.77 (d, 1, H_5), 7.68 (t, 1, H_7), 7.48 (t, 1, H_6), 7.32 (d, 1, H_3), 3.01 (q, 2, J = 7.6 Hz, CH_2), 1.40 (t, 3, J = 7.6 Hz, CH_3); other coupling constants are J_{34} = 8.4 Hz, J_{56} = 8.0 Hz, J_{57} = 1.3 Hz, J_{67} = 6.9 Hz, J_{68} = 1.1 Hz, J_{78} = 8.5 Hz.

15: δ 6.93 (t, 1, H_7), 6.81 (d, 1, H_5), 6.54 (t, 1, H_6), 6.37 (d, 1, H_8), 6.30 (d, 1, H_4), 5.54 (d of d's, 1, H_3), 4.20 (m, 1, H_2), 1.60 (d of t's, 2, J = 7.4 Hz, J = 6.1 Hz, CH_2), 0.96 (t, 3, J = 7.5 Hz, CH_3); other coupling constants are J_{23} = 3.8 Hz, J_{24} = 1.2 Hz, J_{34} = 9.8 Hz, J_{56} = 7.4 Hz, J_{57} = 1.4 Hz, J_{67} = 6.4 Hz, J_{68} = 1.0 Hz, J_{78} = 7.9 Hz.

16: δ 8.92 (br, 1, H_2), 8.11 (resembles overlapping d's, ~2, H_5 and H_8?), 7.69 (resembles a q but perhaps is an overlapping d and t, 2, J = 7.8 Hz, H_3 and H_7?), 7.56 (t, 1, J = 7.1 Hz, H_6?), 3.13 (q, 2, J = 7.6 Hz, CH_2), 1.41 (t, ~3, J = 7.6 Hz, CH_3).

17: δ 7.01 (d, 1, H_5), 6.96 (t, 1, H_7), 6.61 (t, 1, H_6), 6.46 (d, 1, H_8), 3.32–3.22 (c, 2, H_2 and H_2'), 2.64 (m, 1, H_4), 1.90–1.50 (c, 5?, H_3 and H_3', CH_2CH_3, and NH?), 0.98 (t, 3, J = 7.4 Hz, CH_3); other coupling constants are J_{56} = 7.4 Hz, J_{57} = 1.5 Hz, J_{67} = 6.2 Hz, J_{68} = 1.2 Hz, J_{78} = 7.7 Hz.

Reactions with 2-Cyclohexen-1-one. The solutions were prepared in a glovebox. A benzene solution of EtLi was added to a vial containing a diethyl ether solution of Et_2Mg that was stirred with a magnetic stirring bar. Then a diethyl ether solution of 12-crown-4 (0.5 M), when that additive was used, was added and the resulting mixture stirred for 5 min. A diethyl ether solution (0.5 M) of cyclohexenone containing a known amount of undecane as a GC standard was added, resulting in light yellow, turbid solutions. After 4 h, the vial was removed from the glovebox, cooled in ice, and its contents hydrolyzed by addition of a saturated aqueous NH_4Cl solution (5 mL). The aqueous layer was extracted with two 5-mL portions of diethyl ether, which were combined and dried (Na_2SO_4). The "Et_2CuLi" solutions were prepared by addition of the benzene solution of EtLi to CuI in diethyl ether maintained at −15 or −60 °C; after 15 min the cyclohexenone solution was added and the procedure described above was followed. Typical retention times in the GC analyses (column A, 100 °C for 4 min, then programmed at 40 °C/min to a final temperature of 185 °C) were **18** (8.3 min), **19** (8.9), undecane (9.4), and **20** (10.6). Products **18** and **19** were identified by comparison of retention times and mass spectra (GC-MS) with those of authentic samples. Response factors relative to undecane, determined by using standard solutions prepared from authentic samples, were 1.24 for both **18** and **19**, and this factor was assumed for **20**. A sample of the 10.6-min product was collected. Its ^1H NMR spectrum ($CDCl_3$) was virtually identical with that reported above for the 1,3-diethyl-1-cyclohexanol preparation.

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Registry No. 1, 28631-77-8; 2, 536-75-4; 14, 1613-34-9; 15, 126422-62-6; 16, 19020-26-9; 17, 22494-02-6; 18, 115834-53-2; 19, 22461-89-8; 20, 126422-63-7; EtLi, 811-49-4; Et_2Mg, 557-18-6; pyridine, 110-86-1; quinoline, 91-22-5; 2-cyclohexen-1-one, 930-68-7.

Preparation, Characterization, and Reactions of 3-Germabicyclo[3.2.1]octane and 2-Germabicyclo[2.2.1]heptane Derivatives

Anthony G. Sommese and Sheldon E. Cremer*

Department of Chemistry, Marquette University, Milwaukee, Wisconsin 53233

James A. Campbell[1] and Michael R. Thompson

Battelle Pacific Northwest Laboratories, Battelle Boulevard, P.O. Box 999,
Richland, Washington 99352

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Ring closure of the bis-Grignard derived from *cis*-1,3-bis(bromomethyl)cyclopentane (**5**) on R_2GeCl_2 (R = Ph or Me) afforded the 3-germabicyclo[3.2.1]octane system **6** or **7**. Bromine cleavage of a phenyl group in 3,3-diphenyl-3-germabicyclo[3.2.1]octane (**6**) and subsequent nucleophilic displacement of the bromide allowed differing substitution on the germanium atom. Crystals of **6** were grown from 95% ethanol and found to crystallize in the orthorhombic space group $P_{na2}C_A2v$ (No. 33, variation) with $Z = 4$, $a = 7.921$ (2) Å, $b = 31.565$ (5) Å, $c = 6.530$ (2) Å. The refinement cycles resulted in conventional residuals of $R_1 = 0.053$ and $R_w = 0.068$ for the 1483 reflections used. The incorporation of germanium into the bicyclo[2.2.1]heptane system was achieved through a chloroplatinic acid catalyzed, intramolecular hydrogermylation reaction of di-*n*-butyl(3-cyclopentenylmethyl)germane (**14**). The physical and spectral properties of these new molecules are presented.

Introduction

As part of our ongoing studies of bicyclic systems containing heteroatoms,[2-6a] we have targeted the 3-germabicyclo[3.2.1]octane and the 2-germabicyclo[2.2.1]heptane systems for synthetic and stereochemical investigation. Incorporation of germanium into the bicyclic framework posed a synthetic challenge. The 3-germabicyclo[3.2.1]octane and 2-germabicyclo[2.2.1]heptane systems readily lend themselves to stereochemical investigations since one

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