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Reactions of Organomagnesates and Aryl Halides: Metalation and Nucleophilic Substitution

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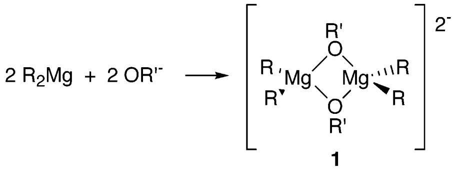
Reactions with aryl halides (ArX) of preparations obtained in diethyl ether from an R_2Mg compound and a cryptand, an alkali-metal alkoxide, or tetrabutylammonium bromide lead to ArH and ArR. ArH results from magnesium−halogen exchange, and ArR results from aryne formation. Reactions of similar preparations with pyridine lead to formation of larger amounts of substitution product, and those with 2-cyclohexen-1-one to larger amounts of 1,4-addition product, than do reactions of R_2Mg alone.

Organomagnesates synthesized from R_2Mg compounds and macrocycles (eq 1)[1−3] and from R_2Mg compounds and alkali-metal alkoxides (eq 2)[4] have been well characterized, and solutions of composition R_3MgM ($M = Na, K$) have been synthesized[4,5] by treating R_2Mg with an alkali metal (eq 3). Organomagnesates react more rapidly with some substrates than do Grignard reagents (RMgX) or R_2Mg compounds—more rapid metalation of acidic hydrocarbons is an example.[6] Even the products can be substantially different. With ketones, for example, organomagnesate preparations furnish an addition product but very much less of the reduction product that often is a significant or even the major product when the organic group of RMgX or R_2Mg has a β-hydrogen.[7]

$$2\,R_2Mg + \text{macrocycle} \longrightarrow R_3Mg^- + RMg(\text{macrocycle})^+ \tag{1}$$



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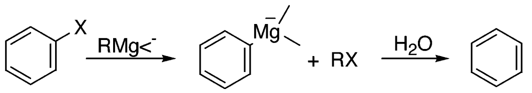
(2)

$$3\,R_2Mg + 2\,K \longrightarrow 2\,R_3MgK + Mg \tag{3}$$

The goal of this study was to investigate reactions of organomagnesates with aryl halides. RMgX and R_2Mg are known to lead to magnesium−halogen exchange with aryl bromides having electron-withdrawing or ortho-chelating groups[8] but not generally otherwise to such exchange with aryl bromides, chlorides, or fluorides. Magnesium−halogen exchange of aryl iodides and Grignard reagents, however, has been developed extensively in the past 3 years, principally by Knochel and co-workers.[8,9] Since our work was completed, reactions of organomagnesate solutions of composition R_3MgLi (prepared from $R_2Mg + RLi$) have been shown by Oshima and co-workers to undergo magnesium−halogen exchange with aryl bromides.[10] Reactions of organomagnesate preparations with pyridine, quinoline, and 2-cyclohexen-1-one also were studied.

Results

Reactions with Aryl Halides. The results indicate that, with preparations thought to contain organomagnesates, aryl halides (ArX) undergo two reactions that are not usual with R_2Mg or RMgX. One reaction, resulting in ArH, is metal−halogen exchange (eq 4). The other reaction, resulting in ArR, is aryne formation (eq 5).



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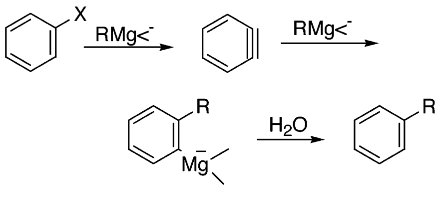

(5)

Reactions with PhX. A PhX compound was added to a preparation obtained from Et_2Mg plus a cryptand

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[1] Partial review: Richey, H. G., Jr. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Eds.; Pergamon: Oxford, U.K., 1996; Vol. 1 (Gokel, G. W., Vol. Ed.), Chapter 21.

[2] Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 432.

[3] At least one R_3Mg^- species is dimeric in the solid (structure **1** with R in place of OR′);[2] no clear evidence indicates whether such aggregation is significant in solution.

[4] Hanawalt, E. M.; Farkas, Jr., J.; Richey, H. G., Jr. *Organometallics* **2004**, *23*, 416.

[5] Malpass, D. B.; Eastham, J. F. *J. Org. Chem.* **1973**, *38*, 3718.

[6] Examples: Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672. Bickelhaupt, F. *Acta Chem. Scand.* **1992**, *46*, 409.

[7] Richey, H. G., Jr.; DeStephano, J. P. *J. Org. Chem.* **1990**, *55*, 3281.

[8] Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414. Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A., Knochel, P. *Synthesis* **2002**, 565.

[9] Rottländer, M.; Boymond, L.; Bérillon, L.; Leprêtre, A.; Varchi, G.; Avolio, S. Laaziri, H.; Quéguiner, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Chem. Eur. J.* **2000**, *6*, 767.

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Table 1. Compositions of Products of Reactions of PhX, Et_2Mg, and an Additive in Diethyl Ether at 25 °C[a]

	amt, %											
	X = I[b]			X = Br[c]			X = Cl[d]			X = F[e]		
additive	PhH	PhEt	PhI	PhH	PhEt	PhBr	PhH	PhEt	PhCl	PhH	PhEt	PhF
none	0	0	95	0	0	99				0	0	100
2,1,1-cryptand	90	6	0	22	13	62	2	0	98			
2,2,1-cryptand	87	5	0	2	0	95	1	0	92			
2,2,2-cryptand	94	0	0	4	0	91	2	0	96			
KOMe[f]	97	0	0	97	2	0	12	81	0	10	80	0
KO-t-Bu	67	12	16	34	14	52	11	43	41	11	48	0
NaOMe[g]	91	0	4	73	3	25	4	29	63	5	37	57
LiOMe	51	0	50	3	0	95	1	0	97			
Li−O-t-Bu	93	0	0	99	2	0	4	30	47	8	33	19
KOPh	95	0	5	99	0	0	3	1	95	6	31	60
NaOPh				62	0	36	1	0	97			

[a] Except where noted, Et_2Mg:PhX:additive was 1:1:1 when the additive was a cryptand and 2:1:4 when it was anything else. Et_2Mg:PhX was 2:1 for reactions without additives. Yields are based on PhX. [b] With PhI, the reaction time was 4.5 h when the additive was a cryptand and 0.5 h for all other reactions. Et_2Mg:PhI:additive was 1:1:2 for reactions with cryptands. Only the reactions with LiO-*t*-Bu and cryptands were completely homogeneous. [c] With PhBr, the reaction time was 23 h for reactions with only two reactants, 4 h when the additive was a cryptand, 1 h when the additive was NaOPh, and 0.5 h when the additive was anything else. Only the reactions with LiO-*t*-Bu and cryptands were homogeneous. [d] With PhCl, the reaction time was 18 h. Only the reactions with LiO-*t*-Bu and cryptands were homogeneous. In the reaction with LiO-*t*-Bu, an ethylbiphenyl (ca. 11%) also was a product. [e] With PhF, the reaction time was 20 h. Only the reaction with LiO-*t*-Bu was completely homogeneous. In the reaction with LiO-*t*-Bu, an ethylbiphenyl (ca. 19%) also was a product. In the reaction with KOMe, an ethylbiphenyl (ca. 4%) also was a product. In the reaction with KO-*t*-Bu, additional products were biphenyl (2%), an ethylbiphenyl (ca. 2%), and a product whose mass spectrum was essentially identical with that of *s*-butylbenzene. [f] A reaction of PhBr and KOMe (1:4) without Et_2Mg gave 0% PhH, 0% PhEt, and 102% PhBr. A similar reaction of PhF gave 0% PhH, 0% PhEt, and 100% PhF. [g] A reaction of PhBr and NaOMe (1:4) without Et_2Mg gave 100% PhBr, 0% PhH, and 0% PhEt.

or an alkoxide or aryloxide salt in diethyl ether. Following hydrolysis, GC analyses showed varying amounts of PhH, PhEt, and recovered PhX (Table 1).[11] An alkoxybenzene was not detected in any reaction. Similar reactions using *only* Et_2Mg, KOMe, or NaOMe led to complete recovery of PhX.[12] Some conclusions are evident from the results. (1) Since no reaction occurs with Et_2Mg alone, the preparations with additives are significantly more reactive. (2) The principal product is PhH from reactions with PhI and PhBr but PhEt from reactions with PhCl and PhF. (3) While with some additives, reaction was substantial with all of the halobenzenes, the reactions using those additives that gave significantly different product yields with different halobenzenes indicate the reactivity order PhI > PhBr > PhCl.[13] The limited results with PhF suggest that it most resembles PhCl in reactivity.

PhH must result from magnesium−halogen exchange (eq 4), so an ethyl halide also should be a product. Ethyl halides were not easily quantified, but the larger alkyl groups of $(octyl)_2Mg$ and $(neopentyl)_2Mg$ facilitated GC analysis: significant amounts of alkyl bromides were obtained from reactions (Table 2) with PhBr of these diorganomagnesium compounds and an alkali-metal alkoxide.[14] That the phenyl product has a Ph−Mg bond before hydrolysis was verified by isolation of $PhCO_2H$ (62% yield) after CO_2 was passed into a PhBr−Et_2Mg−MeOK reaction mixture.

Table 2. Compositions of Products of Reactions of Bromobenzene, R_2Mg, and an Additive in Diethyl Ether at 25 °C[a]

		amt, %			
R	additive	RBr	PhH	PhR	PhBr
octyl	KOMe	42	58	2	0
octyl	NaOMe	28	32	2	53
neopentyl	KOMe	67	85	0	0
neopentyl	LiO-*t*-Bu	80	95	0	0

[a] The reaction time was 3 h. R_2Mg:additive:PhBr was 2:4:1. Only the reaction with LiO-*t*-Bu was completely homogeneous.

Bu_4NBr was the additive for other PhX−Et_2Mg reactions (Table 3). PhH and recovered PhX were obtained, but PhEt was not detected. The reactivity order again was PhI > PhBr > PhCl; indeed, only recovered reactant was obtained from reactions with PhCl. Other reactions of PhCl and PhBr were with solutions prepared from R_2Mg (R = ethyl, neopentyl) and K or Na metal. The results (Table 4) follow the pattern already observed: PhBr was more reactive than PhCl, PhH was the major product from PhBr, and PhR was the major product from PhCl.

NMR Observations with PhX. Observations were of solutions prepared by adding 14N4 (1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) or 211C (2,1,1-cryptand) to benzene-d_6 solutions of R_2Mg and PhI or PhBr. Solutions prepared from *i*-Bu_2Mg, 14N4, and PhI, for example, exhibit the characteristic ^1H NMR absorptions of *i*-$BuMg(14N4)^+$.[15,16] Absorptions characteristic[15,17] of aryl groups in arylmagnesate anions also were

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(10) Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2001**, *66*, 4333. Also see: Iida, T.; Wada, T.; Tomimoto, K.; Mase, T. *Tetrahedron Lett.* **2001**, *42*, 4841.

(11) A small amount of an additional product resulted from some reactions; its mass spectrum is identical with spectra reported for 2-ethylbiphenyl: *TRC Spectral Data*; Hall, H. R., Frenkel, M., Eds.; Thermodynamics Research Center, Texas Engineering Experiment Station, Texas A & M University System: College Station, TX, 1999; spectrum 908. *Eight Peak Index of Mass Spectra*; The Mass Spectrometry Data Centre, Royal Society of Chemistry: Cambridge, U.K., 1991; Vol. 1, Part 1, p 455.

(12) We observed that PhI does not react readily with Et_2Mg in diethyl ether. In contrast, facile reactions have been observed[8,9] of aryl iodides with *i*-PrMgCl in THF. Some combination of the differences in organomagnesium reagent and solvent must be responsible for the different results.

(13) The reaction of Et_2Mg, PhCl, and KOMe (2:1:4) had a half-time of ca. 1.5 h; the corresponding reactions with PhBr and PhI were complete within 0.5 h.

(14) Yields of alkyl halides are somewhat less than of PhH, probably due to reactions of the alkyl halides before hydrolysis. The halides were not contaminants in the R_2Mg reactants: neopentyl *chloride* had been used to prepare the $(neopentyl)_2Mg$ solution, and GC analysis of a hydrolyzed aliquot of the $(octyl)_2Mg$ solution showed 1-bromooctane to be absent.

Table 3. Compositions of Products of Reactions of PhX, Et_2Mg, and $(Bu)_4NBr$ in Diethyl Ether at 25 °C[a]

	rel molar amt			amt, %	
X	Et_2Mg	Bu_4NBr	PhX	PhH	PhX
I	2	0	1	0	95
I	2	1	1	75	15
I	2	2	1	91	8
I	2	10	1	93	0
Br	2	0	1	0	99
Br	2	1	1	6	93
Br	2	2	1	9	92
Br	2	10	1	18	82
Cl	2	1	1	0	97
Cl	2	2	1	0	99
Cl	2	10	1	0	94

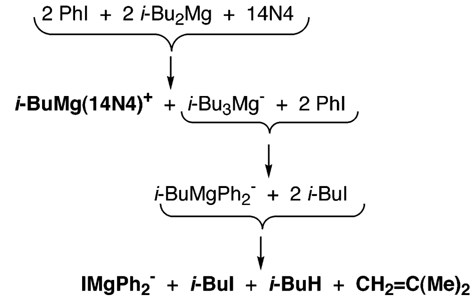
[a] The reaction time was 23 h for reactions without Bu_4NBr, 18 h for the reactions with PhCl, and 4 h for all other reactions. Only the reactions without Bu_4NBr were homogeneous.

Table 4. Compositions of Products of Reactions at 25 °C of PhX with Solutions Prepared from R_2Mg and an Alkali Metal in Diethyl Ether[a]

			amt, %		
X	R	metal	PhH	PhR	PhX
Br	Et	none	0	0	99
Br	Et	K	69	2	30
Br	Np[b]	K	93	0	0
Br	Et	Na	99	0	0
Cl	Et	K	3	16	82
Cl	Et	Na	2	9	89

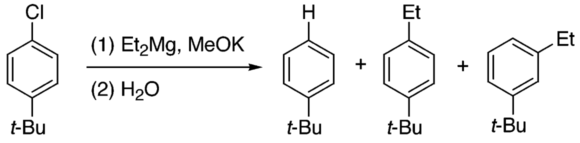
[a] The solutions were prepared using metal:R_2Mg = ca. 5:1. R_2Mg (initial):PhX = 2:1. The reaction time was 23 h for the reaction that did not involve an alkali metal, 2 h for the PhBr−K reactions, and 4−5 h for the other reactions. [b] Neopentyl bromide (85%) also was found in the GC analysis.

Scheme 1



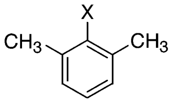
present. The ratio of such aryl groups to i-BuMg(14N4)$^+$ was about 2, so the organomagnesate anion must contain some I (halogen-containing organomagnesate anions have been observed[15] before). Scheme 1 shows a pathway that would lead to the products (shown in bold type); the only other significant ^{1}H NMR absorption is due to a small amount of benzene.[18,19] The cation has an alkyl group, and the aryl groups are in the anion, a preference observed with related organozincate systems.[20] Essentially all PhI in the reactions above had disappeared in the 1 h or so before the first NMR spectra were taken; disappearance of PhBr when used instead of PhI was slower, taking 1−2 days, and no reaction was observed in similar preparations with PhCl. Reactions with PhBr formed product mixtures similar to those with PhI, except that the halide content of the anion was somewhat higher (ca. $PhMgBr_2^-$) and a larger PhH absorption and smaller i-BuH absorptions indicated that elimination of HI from i-BuI to form $CH_2{=}CMe_2$ was due significantly to "Ph$^-$" rather than "i-Bu$^-$". NMR spectra of similar reactions of PhI, $(neopentyl)_2Mg$, and 14N4 or 211C indicated the principal ions to be (neopentyl)Mg(macrocycle)$^+$ and $Ph_{3-x}MgI_x^-$. No alkene and only traces of alkane (neopentane) were present; since the neopentyl group lacks β-hydrogens, the last step in Scheme 1 is not feasible.[21]

Reactions with Substituted Halobenzenes. In a reaction of p-$tert$-butylchlorobenzene (**2**), Et_2Mg, and KOMe (1:2:4), the balance between replacement of Cl by H and by Et was similar to that with PhCl, but *two* ethyl-containing products were obtained. The product composition was 7% *tert*-butylbenzene (**3**), 21% p-ethyl-*tert*-butylbenzene (**4**), and 44% m-ethyl-*tert*-butylbenzene (**5**).



2 **3** **4** **5** (6)

The outcome of reactions of 2,6-dimethylhalobenzenes (**6**), Et_2Mg, and KOMe (1:2:4) depended on the halogen.



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When it was chlorine, the reactant was recovered virtually quantitatively (98%). When it was bromine, however, only a small amount (9%) of reactant was recovered and the principal product was 1,3-dimethylbenzene (91%). The 2,6-dimethyl substitution prevents replacement of chlorine by ethyl but not replacement of bromine by hydrogen.

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[15] Pajerski, A. D.; Chubb, J. E.; Fabicon, R. M.; Richey, H. G., Jr. *J. Org. Chem.* **2000**, *65*, 2231.

[16] Pajerski, A. D. Ph.D. Thesis, The Pennsylvania State University, 1990.

[17] Richey, H. G., Jr.; Kushlan, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 2510.

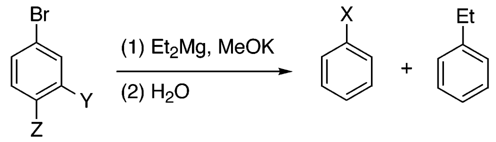
[18] The initial 14N4/PhI ratio was 1:2, and approximately 1 14N4 was evident in NMR spectra of product mixtures. The relative amounts of i-BuI, i-BuH, and $CH_2{=}C(CH_3)_2$ in the product were time-dependent, but the amounts of i-BuH and $CH_2{=}C(CH_3)_2$ were approximately equal and increased as the amount of i-BuI decreased.

[19] Such NMR spectra are remarkably clean; only insignificant absorptions not attributable to the species in Scheme 1 are evident.

[20] Tang, H.; Parvez, M.; Richey, H. G., Jr. *Organometallics* **2000**, *19*, 4810.

[21] As anticipated, reactions of Tol_2Mg (Tol = p-methylphenyl), TolI, and 14N4 (in benzene-d_6 and also in THF-d_8) produced mainly TolMg(macrocycle)$^+$ and Tol_3Mg^-; TolI remained in the solutions. In none of the NMR spectra of diorganomagnesium−macrocycle−aryl halide preparations is there any indication of the presence of Ar−I−R$^-$ or Ar−Br−R$^-$ species which, however, may well have been transient intermediates. Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101. Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1989**, *111*, 3444. Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1991**, *113*, 1414. Beak, P.; Allen, D. J.; Lee, W. K. *J. Am. Chem. Soc.* **1990**, *112*, 1629. Beak, P.; Allen, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 3420. Farnham, W. B.; Calabrese, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 2449. Schulze, V.; Brönstrup, M.; Böhm, P. W.; Schwerdtfeger, P.; Schimeczek, M.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 824.

Reactions were studied of several dihalobenzenes (**7**) with Et_2Mg and KOMe (1:2:4).[22] The product mixtures



(7)

7a Y = F, Z = H	(X = F)	65%	35%
7b Y = H, Z = F	(X = F)	56%	44%
7c Y = Cl, Z = H	(X = Cl)	93%	7%

from *m*- and from *p*-fluorobromobenzene (**7a** and **7b**) contained substantial amounts of PhF and PhEt. PhF presumably results from a reaction of the sort already observed to replace Br by H, and PhEt results from an additional reaction of the sort already observed to convert PhF to PhEt.[23] A reaction of *m*-chlorobromobenzene (**7c**) also provided the product (PhCl) that would result from replacing the more reactive halogen with H and the product (PhEt) that would result from replacing the remaining halogen with ethyl.[24]

Isotope Effect in a Reaction with PhCl. A sample containing equal amounts of C_6D_5Cl and C_6H_5Cl was the substrate for reactions with Et_2Mg−KOMe preparations. The Et_2Mg−KOMe−PhCl stoichiometry was ca. 1:2:1, so that somewhat more than 50% of the mixture of PhCl isotopomers was recovered. The principal product was PhEt (PhEt/PhH = 7.2), as in reactions with isotopically normal PhCl. The ratio of C_6H_5Et and C_6D_4HEt obtained from the parent peaks for these isotopomers in mass spectra indicates $k_H/k_D = 7.5$ (estimates of potential errors in preparing solutions, determining product compositions, and MS analyses indicate that k_H/k_D lies in the range 6.9−8.2).[25]

Mechanisms of Aryl Halide Reactions. That the reactions leading to replacement of halogen of an aryl halide by hydrogen proceed by metal−halogen exchange to produce an arylmagnesium species and an alkyl halide is indicated by (1) NMR observations of ArMg species, (2) observation of the alkyl halide, and (3) the finding that carbonation introduces a carboxyl group. That reactions leading to substitution of the halogen by R proceed principally by an aryne[26] is indicated by (1) the absence of this reaction when methyl groups occupy both positions ortho to the halogen, (2) the formation of positional isomers when the aryl ring has another substituent, and (3) a large H−D isotope effect, consistent with removal of an ortho H being the rate-determining step.[27] The decrease in the ArH/ArR product ratio in the order ArI > ArBr > ArCl > ArF is consistent with competing magnesium−halogen exchange and aryne formation: metal−halogen exchange generally decreases and aryne formation increases in this order.

Reactions with Other Substrates. Although reactions of pyridine with Et_2Mg yield (after hydrolysis) only a trace of 2-ethylpyridine, reactions with some Et_2Mg−macrocycle solutions were earlier found[2,28] to yield significant amounts of both 2- and 4-ethylpyridine.[29] Reactions with preparations that result from combining R_2Mg and an MOR′ compound (M = K, Na, Li), Bu_4NBr, or a $LiNR'_2$ compound are now found also to form both 2- and 4-alkylpyridine; yields are modest but very much greater than with R_2Mg alone. Reactions of quinoline with Et_2Mg yield only 2-ethylquinoline.[29] Reactions of some Et_2Mg−macrocycle solutions with quinoline were earlier found[28] also to yield principally 2-ethylquinoline (small amounts of 4-ethylquinoline also were observed), but these reactions were much faster than reactions with Et_2Mg alone. Reactions of quinoline with Et_2Mg and an MOR′ compound (M = K, Na) are now found to yield only 2-ethylquinoline but also to be faster (at least 100-fold with Et_2Mg−KOMe) than are reactions with Et_2Mg alone.[30] Reactions of Et_2Mg with 2-cyclohexen-1-one result (after hydrolysis) in formation mainly of the 1,2-addition product (1-ethyl-2-cyclohexen-1-ol). Reactions of Et_2Mg−macrocycle solutions, however, were earlier found[28] to give larger amounts of the 1,4-addition product (3-ethylcyclohexanone). Reactions of Et_2Mg−KOR′ preparations are now also found to form larger amounts of the 1,4-addition product. Tables of yields of products from the reactions with pyridine, quinoline, and cyclohexenone are in the Supporting Information.

Although not preparatively useful because of poor yields, these reactions reveal that preparations obtained from R_2Mg and a salt or alkali metal exhibit reactivities similar to those previously observed with R_2Mg−cryptand preparations.

Discussion

Organomagnesates are probably significant reactive species in the reactions with aryl halides, pyridine, quinoline, and 2-cyclohexen-1-one. Benzene (rather than the diethyl ether used in this work) was the solvent for most of the studies that show R_2Mg−macrocycle com-

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[22] The yields obtained from GC analyses fortuitously totaled 100% for each reaction. As elsewhere in this paper, the yields are observed (not normalized) yields.

[23] Replacement of fluorine is far from complete, however. Replacement of bromine must involve a magnesium−halogen exchange. Assuming that the reaction with bromine in large part precedes that with fluorine, then the reaction involving fluorine would be not of PhF but rather of a *p*-fluoromagnesiobenzene (unless this species extracts a proton and is converted to PhF).

[24] A similar reaction of *m*-chlorofluorobenzene yielded PhEt (13%) and two diethylbenzenes (ca. 27% and 60%). Which isomers the diethylbenzenes were was not established; mass spectra were used for identification and are very similar for the three diethylbenzenes. *TRC Spectral Data*; Hall, H. R., Frenkel, M., Eds.; Thermodynamics Research Center, Texas Engineering Experiment Station, Texas A & M University System: College Station, TX, 1999; spectra 439−441.

[25] Since most of the PhCl molecules that react are converted to PhEt (≤10% are converted to PhH), the isotopic composition of recovered PhCl should be approximately the inverse of that of PhEt. This was the case, a confirmation of the analytical procedure.

[26] Reviews of aryne formation and reactions: Hoffman, R. W. *Dehydrobenzene and Cycloalkynes*; Academic: New York, 1967; Chapters 1 and 2. Gilchrist, T. L. In *The Chemistry of Triple-Bonded Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, U.K., 1983; The Chemistry of Functional Groups, Supplement C, Part 1, Chapter 11.

[27] A minor biphenyl product could result from reaction of an organomagnesium product with a second benzyne.

[28] Richey, H. G., Jr.; Farkas, J., Jr. *Organometallics* **1990**, *9*, 1778.

[29] An oxidation also is involved. When the substrate is pyridine, this has always occurred completely before GC analysis. When the substrate is a quinoline, however, a 2-alkyl-1,2-dihydroquinoline also is routinely observed; with exposure of the product to air, this compound gradually diminishes with a concomitant increase of the 2-alkylquinoline.

[30] Reactions with 2-methylquinoline furnish no ethyl-containing products. MS analysis following hydrolysis with D_2O, however, showed substantial incorporation of deuterium in the recovered 2-methylquinoline, indicating that metalation had been significant.

binations to form organomagnesates (e.g., R_3Mg^-); some observations[21,31] indicate that the same species form in diethyl ether.[32] Benzene solutions prepared from an R_2Mg compound and a sufficient amount of NaOMe, KOMe, or other potassium alkoxide salt contain organomagnesates of structure **1**, and observations of KOMe with Et_2Mg, *s*-Bu_2Mg, and Np_2Mg found the same species in diethyl ether.[4,33] Some observations also indicate that organomagnesates (e.g., R_2MgX^-) form when R_2Mg and a tetrabutylammonium halide are combined in benzene and that solutions prepared from R_2Mg and K or Na in benzene generally have the composition R_3MgK or R_3MgNa.[4,33]

It is noteworthy that reactions of phenyl halides with R_2Mg−cryptand or R_2Mg−Bu_4NBr preparations lead to magnesium−halogen exchange but less significantly to benzyne formation. In the reactions of magnesates formed from R_2Mg and MOR′ that lead to substantial benzyne formation, the species abstracting a hydrogen perhaps often is not R but OR′, rendered more reactive by incorporation into an organomagnesate.

Experimental Section

Procedures involving organometallic compounds were performed under an atmosphere of purified nitrogen using Schlenk techniques, a vacuum line, and a glovebox. Solutions for NMR analysis were prepared in a glovebox and transferred into NMR tubes to which an extension of routine glass tubing had been added to facilitate sealing with a flame. An NMR tube was capped temporarily with a septum, removed from the glovebox, immersed in liquid nitrogen, and sealed at the extension.

Reactions of Aryl Halides with R_2Mg−Additive Preparations. The following procedure is typical. A diethyl ether solution of the dialkylmagnesium compound was added dropwise via a syringe to a vial containing diethyl ether and an alkali-metal alkoxide, Bu_4NBr, or macrocycle. The preparation was stirred for a few minutes, and then a diethyl ether solution of the aryl halide and an alkane (as a GC standard) was added. The aryl halide concentration in the reaction preparation was ordinarily ca. 0.1 M. After the preparation was stirred for the desired reaction time, the vial was removed from the glovebox, cooled in an ice bath, and hydrolyzed by addition of a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with two portions of diethyl ether, and the combined diethyl ether extracts were dried (Na_2SO_4). This solution then was subjected to GC analysis. Preparations from R_2Mg and K or Na were filtered through a fritted funnel before the solution of aryl halide was added.

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Supporting Information Available: Text and tables giving full results of reactions with pyridine, quinolines, and 2-cyclohexen-1-one, descriptions of purification of reagents, syntheses of compounds not obtained commercially, GC analyses, product identifications, and NMR spectra of some PhX−R_2Mg−macrocycle preparations. This material is available free of charge via the Internet at http://pubs.acs.org.

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(31) Squiller, E. P. Ph.D. Dissertation, The Pennsylvania State University, 1984. Kushlan, D. M. Ph.D. Dissertation, The Pennsylvania State University, 1987.

(32) Diethyl ether is more convenient than benzene for preparative reactions, since R_2Mg ordinarily is derived from a Grignard reagent (RMgX) prepared in diethyl ether, which must be removed to prepare a benzene solution. For studies involving NMR spectroscopy, however, benzene offers the considerable advantage that its deuterated form is relatively inexpensive.

(33) Organo alkali-metal compounds (RM, M = Li, Na, K) are unlikely to be responsible for the reactions with preparations from R_2Mg and MOR′ (e.g., $R_2Mg + MOR' \rightarrow RMgOR' + RM$?) or an alkali metal (e.g., $R_3MgM \rightarrow R_2Mg + RM$?): such compounds generally react rapidly with diethyl ether, the solvent used for the reactions, and product mixtures obtained from reactions of such compounds with other substrates (e.g., ketones,[7] pyridine, 2-cyclohexen-1-one) are different than those from reactions with R_2Mg−MOR′ preparations.