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Reactions of Dialkylmagnesium–Salt Mixtures with Ketones: Increasing the Ratio of Addition to Reduction

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The reduction of the ketone to a secondary alcohol that accompanies addition in reactions of ketones and dialkylmagnesium compounds can be lessened by first adding an appropriate salt to the dialkylmagnesium compound. With favorable salts and reactant stoichiometries, reduction is eliminated in reactions of dipropylmagnesium with diisopropyl ketone or di-*tert*-butyl ketone. In reactions of di-*tert*-butylmagnesium and di-*tert*-butyl ketone, reduction always predominates, although some addition does occur. Salts observed to have significant effects are potassium methoxide, $(Me_2NCH_2)_2CHOK$, sodium methoxide, lithium methoxide, lithium *tert*-butoxide, tetrabutylammonium bromide, and benzyltriethylammonium chloride. Stoichiometry has significant effects on product composition, the least reduction product generally resulting when the ratio of salt to diorganomagnesium compound is at least one. The fundamental significance of the effects of stoichiometry and of the relative effects caused by different salts is obscured, however, by the heterogeneity of many of the systems. Magnesiate ions, such as $(R_2MgOMe)_2^{2-}$, are thought to be the organomagnesium species responsible for reactions that proceed without reduction.

We recently learned that dialkylmagnesium compounds in the presence of appropriate cryptands disproportionate to form cryptand-coordinated RMg^+ cations and magnesiate anions, such as R_3Mg^- or $R_6Mg_2^{2-}$ (e.g., eqs 1 and 2).[2-4] Such solutions are unusually reactive and in some reactions form products other than those formed by solutions of conventional organomagnesium compounds.

$$2R_2Mg + \text{cryptand} \rightleftarrows RMg(\text{cryptand})^+ + R_3Mg^- \qquad (1)$$

$$2R_3Mg^- \rightleftarrows R_6Mg_2^{2-} \qquad (2)$$

One interesting reaction is with ketones.[3] Reactions of ketones and dialkylmagnesium compounds or Grignard reagents that have β-hydrogens in their alkyl groups ordinarily furnish not only a tertiary alcohol, the conventional addition product, but also the alcohol that results from reduction of the ketone. The much studied reaction (eq 3) of diisopropyl ketone (**1**) and dipropylmagnesium or propyl Grignard reagents is an example.[4-9] The

$$\underset{\mathbf{1}}{(CH_3)_2CHC(O)CH(CH_3)_2} \xrightarrow{R_2Mg} \xrightarrow{H_2O} \underset{\substack{\mathbf{2}:\ R = \text{propyl} \\ \mathbf{3}:\ R = \text{ethyl}}}{(CH_3)_2CHC(OH)(R)CH(CH_3)_2} + \underset{\mathbf{4}}{(CH_3)_2CHC(OH)HCH(CH_3)_2} \qquad (3)$$

amounts of **4** that we observed (first two entries in Table I) are typical. When either the ketone or the organomagnesium compound has somewhat bulkier groups, then the amount of reduction product is larger. When the groups are sufficiently bulky, as in reactions of di-*tert*-butyl ketone (**5**) and *tert*-butylmagnesium compounds,[10] the reduction product (**8**) is formed in good yield and the addition product (**7**) is not even detected.

$$\underset{\mathbf{5}}{(CH_3)_3CC(O)C(CH_3)_3} \xrightarrow{R_2Mg} \xrightarrow{H_2O} \underset{\substack{\mathbf{6}:\ R = \text{propyl} \\ \mathbf{7}:\ R = \textit{tert}\text{-butyl}}}{(CH_3)_3CC(OH)(R)C(CH_3)_3} + \underset{\mathbf{8}}{(CH_3)_3CC(OH)HC(CH_3)_3} \qquad (4)$$

As evident in the third and fourth entries in Table I, some reactions of **1** with solutions of dipropylmagnesium to which cryptands had been added furnished good yields of **2** and no significant amounts of **4**.[3] Magnesiate ions, known to be major components in the solutions, probably are the reactive organomagnesium species. Although magnesiate ions are formed satisfactorily by addition of cryptands to R_2Mg's, this mode of preparation has drawbacks, foremost of which is the extremely high cost of cryptands.[11]

We thought that an alternate procedure for generating ions that might have related activity would be addition to R_2Mg of appropriate salts. Under routine circumstances, organomagnesium compounds do not possess the simple electron-deficient structures (e.g., RMgR, RMgX, etc.) that normally are written for them. Mg is generally found to be 4–7-coordinate in crystal structures of organomagnesium compounds,[12] and it is likely that coordination in solution usually falls into the same range. The extra bonds to the magnesium of an organomagnesium compound are provided by some combination of bridging

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[6] Chastrette, M.; Amouroux, R. *Bull. Soc. Chim. Fr.* **1970**, 4348.

[7] Georgoulis, C.; Gross, B.; Ziegler, J.-C. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1971**, *273*, 378.

[8] Ziegler, J.-C. Doctoral Dissertation, L'Universitē de Nancy I (undated).

[9] Whitmore, F. C.; George, R. S. *J. Am. Chem. Soc.* **1942**, *64*, 1239.

[10] Singer, M. S.; Salinger, R. M.; Mosher, H. S. *J. Org. Chem.* **1967**, *32*, 3821.

[11] The most favorable cryptand for causing disproportionation, 2,1,1-cryptand, currently costs (USA) $61,000 a mole (Aldrich Chemical Co.). Our efforts at preparing this compound suggest that this price may be reasonable.

[12] One exception is the planar trineopentylmagnesiate anion [ref 2]. Trivalent magnesium is found also in a highly hindered environment [Engelhardt, L. M.; Jolly, B. S.; Junk, P. C.; Raston, C. L.; Skelton, B. W.; White, A. H. *Aust. J. Chem.* **1986**, *39*, 1337].

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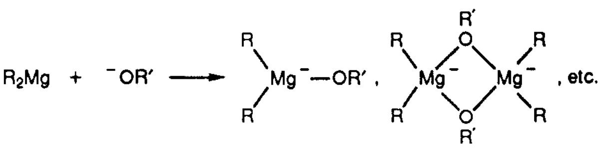
Table I. Yields of Products from Reactions of Dipropylmagnesium, Diisopropyl Ketone (1), and Salts in Diethyl Ether at 25 °C[a]

	rel molar amounts[c]			yields[d]		
salt[b]	salt	R_2Mg	1	**2**, %	**4**, %	**1**, %
none	0	1	0.5	72 (58)	25 (26)	4 (3)
none	0	1	1	52 (42)	44 (38)	4 (9)
2,1,1-cryptand[e]	1	1	0.5	81	0	10
2,2,2-cryptand[e]	0.5	1	0.5	87	0.1	0
MeOK	2	0.5	1	7 (8)	0 (0)	74 (56)
MeOK	2	1	1	60 (63)	0 (0)	36 (39)
MeOK	2	1	0.5	86 (85)	0 (0)	13 (16)
MeOK	1	1	1	48 (49)	0 (0)	42 (28)
MeOK	1	1	0.5	53 (57)	0 (0)	9 (2)
MeOK	0.5	1	1	43	27	20
MeOK	0.5	1	0.5	69	8	0
MeOK	0.25	1	1	39 (42)	36 (30)	22 (22)
MeOK	0.25	1	0.5	65	10	0
MeOK	0.125	1	1	34	38	20
t-BuOK	2	1	1	0 (0)	0 (0)	98 (95)
PhOK	2	1	1	20	0	70
PhOK	2	1	0.5	43	8	43
$(Me_2NCH_2)_2CHOK$	1	1	0.25	48	0	49
MeONa	2	1	1	50	38	7
MeONa	2	1	0.5	88	10	0
MeONa	2	1	0.25	74	14	0
MeONa	1	1	0.25	83 (82)	2 (3)	0 (0)
MeONa	1	1	0.125	84 (85)	0 (0.8)	0 (0)
MeONa	0.5	1	0.25	78	6	5
MeOLi	2	1	1	51	41	5
MeOLi	2	1	0.5	74	22	0
MeOLi	2	1	0.25	63	26	2
MeOLi	1	1	0.25	67	16	2
MeOLi	1	1	0.125	67	7	0.7
t-BuOLi	2	1	1	72 (55)	0 (0)	18 (22)
t-BuOLi	2	1	0.5	97	0	0
t-BuOLi	1	1	1	57	12	22
t-BuOLi	1	1	0.5	84	1.7	0.2
t-BuOLi	0.5	1	1	61	23	5
t-BuOLi	0.5	1	0.5	80	5	0.4
Bu_4NBr	1	1	1	54	27	4
Bu_4NBr	1	1	0.5	79	7	0.9
Bu_4NBr	1	1	0.25	84 (79)	0 (0)	0 (0)
Bu_4NBr	0.4	1	1	50	26	6
Bu_4NBr	0.4	1	0.5	74	8	0.6
Bu_4NBr	0.2	1	1	49	28	5
Bu_4NBr	0.2	1	0.5	68	8	1.1
$BzlEt_3NCl$	1	1	0.5	57 (47)	28 (32)	1.6 (4)
$BzlEt_3NCl$	1	1	0.5[f]	41	13	26
$BzlEt_3NCl$	1	1	0.25	68 (67)	0 (0)	0.2 (0)

[a] Reaction times were 1 h. [b] The R_2Mg–salt preparations with MeOK, t-BuOK, PhOK, MeONa, MeOLi, Bu_4NBr, and $BzlEt_3NCl$, to which the ketone then was added, generally were suspensions, those with Bu_4NBr having a gellike mass at the bottom of a solution. The other R_2Mg–salt preparations were essentially homogeneous. [c] If all parts of the initial R_2Mg remained in solution, then the concentration of "R_2Mg" was 0.065–0.085 M. [d] Yields are based on **1**. A yield of 0 indicates <0.1%. Numbers in parentheses are the results of duplicate, independent experiments. [e] Results taken from ref 3. [f] Half of the ketone was added initially. After 1 h the other half was added, and the reaction was allowed to proceed for an additional 1 h.

groups (e.g., halogens and alkyl groups) and coordination by solvent atoms with unshared electron pairs (e.g., ether oxygens and tertiary amine nitrogens). Since anions are considerably better electron donors than the corresponding neutral species, it seems likely, as illustrated in eq 5 for



(5)

9

an alkoxide anion, that addition of appropriate anions will lead to formation of magnesiate ions. In other work we have been trying to define the species formed when salts are added to organomagnesium compounds, and have found **9** to be the probable structure for a prominent species in solutions prepared from R_2Mg and KOR′ or NaOR′.[13] In fact, Ashby, Arnott, and Srivastava earlier concluded that the major species in solutions formed from equimolar amounts of KH and dialkylmagnesium compounds had structures corresponding to **9** (H in place of OR′).[14,15]

When we began this work we were aware of just two closely related publications. Chastrette and Amouroux had studied effects of lithium and tetrabutylammonium halides on reactions of **1** and propylmagnesium bromide, and found that the product mixtures had increased **2**:**4** ratios,

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[13] Hanawalt, E. M.; Richey, H. G., Jr., submitted for publication in J. Am. Chem. Soc. and unpublished results.

[14] Ashby, E. C.; Arnott, R.; Srivastava, S. Inorg. Chem. 1975, 14, 2422.

[15] Vibrational spectra of solids formed from tetramethylammonium salts and dimethylmagnesium have been interpreted to indicate that some have structures in which bridging is only by methyl groups and others have structures in which bridging is both by anions of the salt and by methyl groups [Klopsch, A.; Dehnicke, K. Chem. Ber. 1975, 108, 420. Müller, J.; Schmock, F.; Klopsch, A.; Dehnicke, K. Chem. Ber. 1975, 108, 664].

Table II. Yields of Products from Reactions of Dipropylmagnesium, Di-*tert*-butyl Ketone (5), and Salts in Diethyl Ether at 25 °C[a]

	rel molar amounts[c]			yields[d]		
salt[b]	salt	R_2Mg	5	6, %	8, %	5, %
none	0	1	0.5	1.3	88	0.7
none	0	1	1	0.9	92	0.8
MeOK	2	1	0.5	85	0	0
MeOK	1	1	0.5	81	0	0
$PhCH_2OK$	1	1	0.25	20	2	77
$(Me_2NCH_2)_2CHOK$	1	1	0.25	79 (83)	0 (0)	0 (0)
MeONa	2	1	0.5	8	72	10
MeONa	2	1	0.25	6	78	3
MeONa	1	1	0.5	2	79	0
t-BuOLi	2	1	0.5	81	0	0
t-BuOLi	1	1	0.5	84	0	0
Bu_4NBr	2	1[e]	1	3	38	47
Bu_4NBr	2	1[e]	0.5	5	59	17
Bu_4NBr	1	1	0.5	6	72	14
Bu_4NBr	1	1	0.125	7	74	0
$BzlEt_3NCl$	1	1	0.5	2	77	8
$BzlEt_3NCl$	1	1	0.125	3	71	0

[a] Reaction times were 1 h. [b] The R_2Mg–salt preparations with $PhCH_2OK$, MeONa, Bu_4NBr, and $BzlEt_3NCl$, to which the ketone then was added, generally were suspensions, those with Bu_4NBr having a gellike mass at the bottom of a solution. The other R_2Mg–salt preparations were essentially homogeneous. [c] If all parts of the initial R_2Mg remained in solution, then the concentration of "R_2Mg" was 0.065–0.085 M except in the two cases that are noted. [d] Yields are based on 5. A yield of 0 indicates <0.1%. Numbers in parentheses are the results of a duplicate, independent experiment. [e] The concentration of "R_2Mg" was 0.03–0.04 M.

although 4 always remained a significant product.[6] These workers also found that addition of tetrabutylammonium halides increased the ratios of addition product to reduction product in reactions of benzaldehyde with organozinc[16] and organoaluminum[17] compounds, although reduction product was not eliminated. Georgoulis, Gross, and Ziegler had reported the effects of *t*-BuOK on reactions of dipropylmagnesium and 1.[7] Formation of 4 was not significant, but a large amount of 1 was recovered when equimolar amounts of Pr_2Mg, 1, and the salt were used. It was assumed that the recovered 1 represented a ketone that had been metalated by the organomagnesium solution and in that way protected against addition. After most of the work reported in this paper was completed, we learned that a thesis[8] by Ziegler contained some additional, relevant results, that will be mentioned in the Results and Discussion.

Effects of salts, most commonly lithium or tetraalkylammonium halides and perchlorate, have been studied on other reactions of organomagnesium compounds, but generally have been small. Studies have been of the stereochemistry (cis or trans) of product mixtures formed by additions to saturated cyclic ketones,[18] the diastereomer ratios resulting from additions to aldehydes with chiral α-carbons,[19] the rates of addition to a nitrile[20] and an imine,[21] the ratio of addition to metalation of a nitrile,[22] and the structures and stereochemistries of polymers formed using organomagnesium initiators.[23]

Results and Discussion

Organomagnesium–salt mixtures were prepared by adding a diethyl ether solution of a dialkylmagnesium compound to a stirred diethyl ether suspension containing varying amounts of a salt. After a few minutes a diethyl ether solution of the ketone was added. As noted in Tables I–III, considerable amounts of solid or gellike material often were present at the time that the ketone solution was added. Following hydrolysis, the reaction mixtures were analyzed by gas chromatography.

The results reported in Table I for the reaction of 1 with dipropylmagnesium indicate that most salts that were tried could diminish the amount of reduction product 4. The extent to which 4 was eliminated depended on the particular salt and the relative amounts of salt and organomagnesium compound. In a number of experiments 4 was insignificant (<0.1%). Similar observations were made in reactions of 5 with dipropylmagnesium, reported in Table II. Elimination of reduction product 8 in some reactions of 5 is particularly striking, since in the absence of salts product mixtures contained mainly this compound. A decrease in reduction product also was found in reactions of 5 and di-*tert*-butylmagnesium, reported in Table III. While the yield of addition product 7 never was large, *this product was not detected at all in the absence of salts.*[10]

The results indicate that the conjecture that addition of salts to diorganomagnesium compounds might have effects similar to additions of cryptands was correct. Some generalizations can be made on the basis of the data reported in Tables I–III. (1) The ability of salts to decrease the reduction product is greatest for the reaction of dipropylmagnesium with 1 and least for the reaction of di-*tert*-butylmagnesium with 5. In these examples, the less reduction product formed in the absence of a salt, the more likely it is to be eliminated by addition of salts. (2) The effect of a particular salt on the addition to reduction ratio can depend significantly on reactant ratios. The ratio of addition to reduction tends to increase with increasing ratios of salt to R_2Mg and of R_2Mg to ketone. Some reduction product was seen in almost all reactions in which the salt to R_2Mg ratio was <1. In some instances, however, a salt to R_2Mg ratio of 2 leads to less reduction than does a ratio of 1. (3) Salts differ in their effectiveness to influence the addition to reduction ratio. MeOK, $(Me_2NCH_2)_2CHOK$, and *t*-BuOLi, for example, seem generally to be more effective than MeONa, Bu_4NBr, or $BzlEt_3NCl$.

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(16) Chastrette, M.; Amouroux, R. *Tetrahedron Lett.* **1970**, 5165.

(17) Chastrette, M.; Amouroux, R. *J. Organomet. Chem.* **1974**, *70*, 323.

(18) Chastrette, M.; Amouroux, R. *Bull. Soc. Chim. Fr.* **1974**, 1555. Ashby, E. C.; Chao, L.-C.; Laemmle, J. *J. Org. Chem.* **1974**, *39*, 3258. Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4371.

(19) Yamamoto, Y.; Matsuoka, K. *J. Chem. Soc., Chem. Commun.* **1987**, 923.

(20) Chastrette, M.; Amouroux, R.; Subit, M. *J. Organomet. Chem.* **1974**, *78*, 303.

(21) Thomas, J. *Bull. Soc. Chim. Fr.* **1975**, 209.

(22) Chastrette, M.; Amouroux, R.; Subit, M. *J. Organomet. Chem.* **1975**, *99*, C41.

(23) For example, see the following and references cited therein: Hsieh, H. L.; Wang, I. W. *Macromolecules* **1986**, *19*, 299.

Table III. Yields of Products from Reactions of Di-*tert*-butylmagnesium, Di-*tert*-butyl Ketone (5), and Salts in Diethyl Ether at 25 °C

	rel molar amounts[b]			yields[c]		
salt[a]	salt	R_2Mg	5	7, %	8, %	5, %
none[d]	0	1	0.5	0	74	32
none[d]	0	1	0.25	0	73	30
MeOK[e]	4	1[f]	0.5	7	17	36
MeOK[d]	1	1	0.5	0	69	24
MeOK[d]	1	1	0.25	0	72	16
t-BuOLi[e]	4	1[f]	0.5	0.3	0	84
t-BuOLi[d]	2	1	0.5	14	39	65
t-BuOLi[e]	2	1	0.5	12	30	67
t-BuOLi[d]	1	1	0.5	3 (5)	69 (37)	41 (29)
t-BuOLi[e]	1	1	0.5	6	91	14
t-BuOLi[d]	1	1	0.25	7	71	15
t-BuOLi[e]	1	1	0.25	3	102	0
t-BuOLi[d]	1	1	0.125	5	66	8
t-BuOLi[e]	1	1	0.125	7	81	0

[a] Most of the R_2Mg–salt preparations, to which the ketone then was added, were essentially homogeneous. [b] If all parts of the initial R_2Mg remained in solution, then the concentration of "R_2Mg" was 0.06–0.07 M except in the one case noted. [c] Yields are based on **5**. A yield of 0 indicates <0.1%. Numbers in parentheses are the results of a duplicate, independent experiment. [d] Reaction time was 1 h. [e] Reaction time was 24 h. [f] The concentration of "R_2Mg" was 0.03–0.04 M.

Ziegler's thesis[8] describes some related experiments. In reactions of dipropylmagnesium and **1**, he studied the effects of several alkali metal alkoxide, enolate, and other salts. Reduction was often diminished, though eliminated only in the reaction with *t*-BuOK already referred to,[7] in some reactions with Ph_3CK, and in single reactions with $CH_3OCH_2CH_2OCH_2CH_2OK$ and Ph_3CLi. In other reactions, however, the ratio of salt to organomagnesium compound that was used often was considerably less than 1, and in some of these reactions, reduction product was not produced during the addition of the first portions of the ketone.

To define what organomagnesium species are responsible for the reaction behavior of the R_2Mg–salt preparations will require much more information. Identifying the major organomagnesium species present in such preparations is not sufficient, since even a minor species that equilibrates with more major species at a sufficiently rapid rate might be responsible for the reaction products. The heterogeneity of many of the R_2Mg–salt preparations is an additional complicating factor. A salt could be ineffective, for example, simply because it or a magnesiate species it forms is particularly insoluble.

It seems most likely that the reactions are due to magnesiate species, such as **9**. The possibility that the reactive species are organoalkali compounds, formed as in eq 6, must also be considered. That organoalkali compounds

$$R_2Mg + MeOK \rightleftarrows RK + RMgOMe \tag{6}$$

$$RLi + t\text{-BuOK} \rightleftarrows RK\downarrow + t\text{-BuOLi} \tag{7}$$

might form is not improbable; as illustrated in eq 7, it is well established that *t*-BuOK and RLi form precipitates which are mainly RK.[24] For the following reasons, however, we do not think that the product mixtures we observe generally result from reactions of organoalkali compounds. (1) Alkylpotassium compounds rapidly abstract a proton from diethyl ether and hence are destroyed in that solvent.[25] The organometallic species present in many R_2Mg–potassium salt systems, however, are stable for hours in diethyl ether.[26] (2) Tetraalkylammonium halides salts can greatly enhance the ratio of addition to reduction. These salts cannot form alkali metal organometallic compounds. (3) Alkylpotassium compounds probably react with ketones more to produce metalation and reduction products than addition products. A reaction of **1** and EtK (prepared from Et_2Hg and Na–K alloy) furnished 44% of **1**, 7% of **2**, and only 2% of the addition product, **3**, and so proceded mainly by metalation. It has been reported that reactions of phenylpotassium and acetophenone result in approximately 10:1 ratios of metalation to addition.[27] It also has been reported that reactions of pentylpotassium and benzaldehyde, a carbonyl compound lacking α-hydrogens, lead to more reduction than addition.[28,29] (4) Reactions of some other substrates with solutions and mixtures obtained from alkali metal salts and R_2Mg's do not give the product mixtures expected for reactions of the corresponding organoalkali compounds.[13,30]

The results could be due to magnesiate ions, such as R_3Mg^-, that do not incorporate an anion from the salt. Such magnesiate ions could be formed by disproportionation (e.g., eq 8) or due to insolubility of the Mg salt incorporating the anion of the added salt (e.g., eq 9). NMR

$$2R_2MgZ^- \rightleftarrows R_3Mg^- + RMgZ_2^- \tag{8}$$

$$3R_2Mg + MZ \rightleftarrows 2R_3Mg^-M^+ + MgZ_2\downarrow \tag{9}$$

studies,[13] to be published elsewhere, suggest that the anions formed from mixing R_2Mg's and salts generally incorporate

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[24] For example, see the following and earlier references cited therein: Pi, R.; Bauer, W.; Brix, B.; Schade, C.; Schleyer, P. v. R. *J. Organomet. Chem.* **1986**, *306*, C1. Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1987**, *326*, 1.

[25] Ebel, H. F.; Lüttringhaus, A. *Method. Org. Chem.* (*Houben-Weyl*), *4th Ed.* **1970**, *13* (part 1), 255.

[26] Failure to observe attack on diethyl ether rules out the presence of significant amounts of organopotassium compounds before addition of the ketone. It does not exclude the possibility that an organopotassium compound forms after addition of the ketone and reacts more rapidly with the ketone than with diethyl ether. For organopotassium compounds generated after ketone addition to have contributed significantly to product formation in the reactions reported here, however, would require that generation of an organopotassium compound be significantly more rapid in the presence of the ketone than in its absence.

[27] O'Sullivan, W. I.; Swamer, F. W.; Humphlett, W. J.; Hauser, C. R. *J. Org. Chem.* **1961**, *26*, 2306.

[28] Gordash, Yu. T.; Bogatchenko, G. S.; Chernyshev, I. A.; Klimenko, P. L. *J. Org. Chem. USSR* (*Engl. Transl.*) **1975**, *11*, 533.

[29] The organopotassium compounds in the reactions that have been studied with ketones, however, are solids suspended in hydrocarbons. It is possible that an organopotassium compound in this form may react differently than one that might be generated in diethyl ether from R_2Mg and a salt [ref 26] and react before it coalesced into particulate material.

[30] For example, addition of lithium salts to R_2Mg followed by addition of pyridine leads to attachment of R both at C-2 and C-4 of pyridine; addition of pyridine to RLi results in attachment of R only at C-2 [ref 13].

the anion of the salt.[31] It cannot be ruled out, however, that species such as R_3Mg^- are minor components and perhaps responsible for formation of at least portions of the reaction products.

Since some R_2Mg is likely to remain in some of the R_2Mg–salt preparations, the fact that so many preparations produce no reduction product suggests that addition to ketones of the new reactive species formed in this way is very much faster than addition of R_2Mg. In fact, Ziegler found that *t*-BuOK and *t*-BuOLi can accelerate addition 200-fold in reactions of **5** and dimethylmagnesium, an organomagnesium compound that lacks β-H's and leads only to addition.[8]

Considerable amounts of the ketone reactant were recovered from some reactions. Two reactions of *t*-BuOK, dipropylmagnesium, and **1** (2:1:1) in which only **1** was observed in the product mixture were hydrolyzed with D_2O. Mass spectra indicated that approximately 50% of the recovered **1** was monodeuterated and approximately *30% was dideuterated*. Therefore, most of the recovered ketone had undergone metalation rather than no chemical change. Other work has indicated that the magnesiate species formed from R_2Mg and a crown ether can metalate an acidic hydrocarbon more rapidly than does R_2Mg alone.[32] In the absence of isotopic information, it is not certain that all other instances where recovery of ketone was significant also are due to metalation by R groups of organomagnesium species. In some cases sufficient R groups to permit reaction with all of the ketone may not have been present in an active form. Active R groups could be destroyed by protonation by water, other impurities in the salts, or solvent hydrogens. In reactions that are heterogeneous, it also is possible that some R groups are in a form so insoluble that they are effectively precluded from reacting with the ketone.

There is yet no definitive evidence concerning mechanistic features of the additions. Transfer of an electron from a magensiate ion to the ketone is a possible initial step, however. Electron transfer has been proposed[33] to be the initial step in some reactions of ketones and conventional organomagnesium compounds in which these reactants have favorable structural features, and magnesiate ions should be better electron donors than are neutral organomagnesium compounds. Coordination of a ketone to magnesiate ions should be less favorable than to conventional organomagnesium compounds. If such coordination is required for reduction, as has sometimes been proposed,[34] then reduction would be slowed. For the reactions of **5** with Et_2Mg, which leads to reduction plus addition in the presence of *t*-BuOK but only to reduction in its absence, Ziegler concluded that the rate of reduction is considerably less in the presence of *t*-BuOK than in its absence.[8]

Whatever the reactive species and mechanisms may prove to be, addition of salts to dialkylmagnesium compounds can greatly reduce the amount of reduction product formed in reactions with ketones.

Experimental Section

Materials. Diethyl ether was dried over sodium and then distilled from sodium benzophenone ketyl under an atmosphere of nitrogen.

(a) Organomagnesium Compounds. A solution of propyl bromide (freshly distilled, 10.9 mL, 0.12 mol) in diethyl ether (30 mL) was added over 2 h to a suspension of magnesium pieces (Cerac 99.99%, 4.9 g, 0.20 mol) in diethyl ether (80 mL) maintained under a nitrogen atmosphere. The mixture was then stirred for an additional 12 h. A solution of dioxane (11.9 mL, 0.14 mol) in diethyl ether (30 mL) was added over 2 h, and the suspension was stirred for 12 h. The suspension was centrifuged, and the supernatant solution was carefully removed. If much clouding developed on addition of silver nitrate to a hydrolyzed aliquot, indicating the presence of significant bromide, then the solution was not used. The concentration of dipropylmagnesium, generally about 0.4 M, was determined by adding an aliquot to water, followed by addition of an excess of a standard aqueous HCl solution and titration with a standard aqueous NaOH solution to a bromothymol blue endpoint. Solutions of di-*tert*-butylmagnesium, generally about 0.20 M, were prepared in a similar fashion from *tert*-butyl chloride and magnesium (J. T. Baker).

(b) Salts. MeOK, MeONa, MeOLi, and *t*-BuOLi (sublimed at reduced pressure) were commercial samples (Alfa); so were *t*-BuOK (sublimed at reduced pressure), Bu_4NBr (heated at 135 °C for at least 5 h prior to use), and $BzlEt_3NCl$ (Aldrich). PhOK,[35] $(Me_2NCH_2)_2CHOK$, and $PhCH_2OK$ were prepared and provided by Julius Farkas.

(c) Organic Reactants and Products. Ketones **1** (Aldrich) and **5** (Fluka) and alcohol **4** (Aldrich) were commercial samples and were redistilled. Alcohol **2** was available by a standard Grignard reaction.[9] Alcohol **7** was prepared from hexamethylacetone and *tert*-butyllithium in a manner similar to that already described.[36] Since *tert*-butyllithium is available commercially as a solution in pentane, however, pentane instead of diethyl ether was used as the solvent; moreover, the reaction could be carried out successfully at room temperature instead of −60 °C since attack of the organolithium compound on the hydrocarbon solvent is not a problem. Samples of **6** and **8**, whose structures were confirmed by their ^1H NMR spectra, were isolated from reactions similar to those described below by using glass U-shaped tubes inserted into the exit port of the gas chromatograph and cooled in liquid nitrogen. A gas chromatograph with a thermal conductivity detector was used for the sample collections; the column was similar to that used for analysis of reaction mixtures.

Procedures for Reactions of Et_2Mg–Salt Preparations and Ketones. The reaction solutions were prepared in a glovebox under a nitrogen atmosphere using glassware that had been dried in an oven at 120 °C. A portion of the salt was weighed into a flask containing a magnetic stirring bar, and diethyl ether (5 mL) was added. A serum cap was placed on the flask, the mixture was stirred for about 5–10 min, and then the solution of dialkylmagnesium compound was added slowly with a syringe while stirring continued. Ordinarily the amount of stock dialkylmagnesium solution was used that contained 0.5 mmol of the dialkylmagnesium compound. Then a diethyl ether solution (~0.5 M) of the ketone (freshly distilled) and the alkane standard (Aldrich) was added. The reaction mixture was allowed to stir for the indicated time and then was cooled in an ice bath and quenched with a saturated aqueous solution of ammonium chloride. The ether layer was separated (no drying agent used) and used for the product analysis.

Product Analysis. Reaction mixtures were analyzed by gas chromatography using a chromatograph with a flame ionization detector, helium as the carrier gas, and a glass column, 0.25 in. × 10 ft, packed with 3% SP2100 on Supelcoport (100–120 mesh). Products were identified by comparing their retention times and electron-impact mass spectra (obtained using a gas chromatograph with a column similar to that used for analysis attached to a Finnigan 3200 mass spectrometer) with those of authentic samples. Mass spectra of the **1** obtained from the reactions hydrolyzed with D_2O were obtained using the same apparatus. Products were

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(31) Reactions of KH with various R_2Mg's sometimes are exceptions. Solutions ultimately can result with a composition close to R_3MgK, presumably by precipitation of MgH_2 [ref 13].

(32) For an example, see Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672.

(33) For a brief review of potential electron-transfer reactions involving organomagnesium compounds, see: Eberson, L. *Electron Transfer Reactions in Organic Chemistry*; Springer-Verlag: Berlin, 1987; Chapter 8.

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detectable down to levels corresponding to yields of approximately 0.1%. Any peak whose area never represented more than 2% of the total area due to all product peaks was not investigated. Peak areas were determined using a Varian CDS 111L integrator. Yields were determined by comparisons of areas of absorption for each component relative to that of an alkane standard. For the reaction of 1 with dipropylmagnesium, undecane was the internal standard and the GC conditions were 2 min at 45 °C followed by an increase of 50 °C per min to 130 °C, which temperature then was maintained. Retention times (min) and response factors (for equal weights) were **1** (1.52, 1.38), **4** (1.97, 1.20), undecane (3.68, 1.00), and **2** (4.17, 1.08). For the reactions with **5**, it was assumed that the detector responded equally to equal weights of different compounds. For the reaction with dipropylmagnesium, pentadecane was the internal standard and the GC conditions were 2 min at 55 °C followed by an increase of 55 °C per min to 160 °C, which temperature then was maintained. Retention times (min) were **5** (2.20), **8** (2.79), **6** (4.25), and pentadecane (5.40). For the reaction with di-*tert*-butylmagnesium, hexadecane was the internal standard and the GC conditions were 45 °C for 3 min followed by an increase of 60 °C per min to 200 °C, which temperature then was maintained. Retention times (min) were **5** (2.80), **8** (3.81), **7** (5.91), and hexadecane (6.53).

Reaction of Ethylpotassium and 1. A sample of Na–K alloy prepared[37] by pushing together Na (0.15 g, 6.5 mmol) and K (0.78 g, 20 mmol) was added to cyclohexane (10 mL). To the stirred suspension was added dropwise over 15 minutes a solution of Et_2Hg (1.68 g, 6.5 mmol) in cyclohexane (3 mL), and the resulting mixture was stirred for 24 h. Excess alloy was removed by addition of mercury,[38] stirring for 2 h, and decanting the suspension of EtK from the solid. Decane (as a GC standard) and **1** (0.24 g, 2.1 mmol) were added to this suspension. The reaction mixture was stirred for 18 h and quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried (Na_2SO_4). GC conditions were similar to those reported for reactions of **1** above; a response factor of 1.1 was assumed for **3**.

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Registry No. **1**, 565-80-0; **2**, 51200-81-8; **3**, 3970-59-0; **4**, 600-36-2; **5**, 815-24-7; **6**, 32579-69-4; **7**, 41902-42-5; **8**, 14609-79-1; EtK, 4522-40-1; Et_2Hg, 627-44-1; Pr_2Mg, 4907-44-2; $t\text{-}Bu_2Mg$, 14627-81-7; MeOK, 865-33-8; *t*-BuOK, 865-47-4; PhOK, 100-67-4; $(Me_2NCH_2)_2CHOK$, 126083-47-4; MeONa, 124-41-4; MeOLi, 865-34-9; *t*-BuOLi, 1907-33-1; Bu_4NBr, 1643-19-2; $BzlEt_3NCl$, 56-37-1; $PhCH_2OK$, 22379-62-0; 2,1,1-cryptand, 31250-06-3; 2,2,2-cryptand, 23978-09-8; propyl bromide, 106-94-5; *tert*-butyl chloride, 507-20-0.

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Estimation of Free Radical Group Enthalpy of Formation Values. Application to Estimation of Bond Dissociation Energies in Perfluoroalkylbenzenes

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A correlation has been observed between the differences in Benson's group enthalpies of formation for free radicals, $\{[{}^{\bullet}\text{C-(X)(Y)(Z)}] - [{}^{\bullet}\text{C-(H)(Y)(Z)}]\}$, and the related molecules, $\{[\text{C-(H)(X)(Y)(Z)}] - [\text{C-(H)}_2\text{(Y)(Z)}]\}$, where X = C, C_B, C_d, C_t, CN, CO, Br, Cl, F, I, N, NO_2, O, or Si, and Y and Z = H or the same X atoms or groups except Si. The least squares equation, $[{}^{\bullet}\text{C-(X)(Y)(Z)}]$ (kcal mol^{-1}) = $[{}^{\bullet}\text{C-(H)(Y)(Z)}] + (0.857 \pm 0.031)\{[\text{C-(H)(X)(Y)(Z)}] - [\text{C-(H)}_2\text{(Y)(Z)}]\} - (4.64 \pm 0.62)$, $r^2 = 0.90$, $n = 89$, provides a way to estimate unknown radical group values when the other three group values in the equation are known. Numerous new radical group values were derived from experimental enthalpies of formation for use in this correlation. Analogous equations were also derived for the specific cases where X is only one of the atoms or groups indicated. Applications of these equations for estimating the benzylic bond dissociation energies for the perfluoroalkylbenzenes are reported; $D(PhCF_2{-}R_f)$ = 112, 78, and 70 kcal mol^{-1} for R_f = F, CF_3, and CF_2CF_3, respectively.

Introduction

Benson and co-workers have developed a useful method for predicting enthalpies of formation of molecules and free radicals from constituent group values.[1] The utility of this method for free radicals is limited because of the lack of many of the required group values, $[{}^{\bullet}\text{C-(X)(Y)(X)}]$. In the course of another research project where we needed to estimate the enthalpies of formation of several halogenated

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