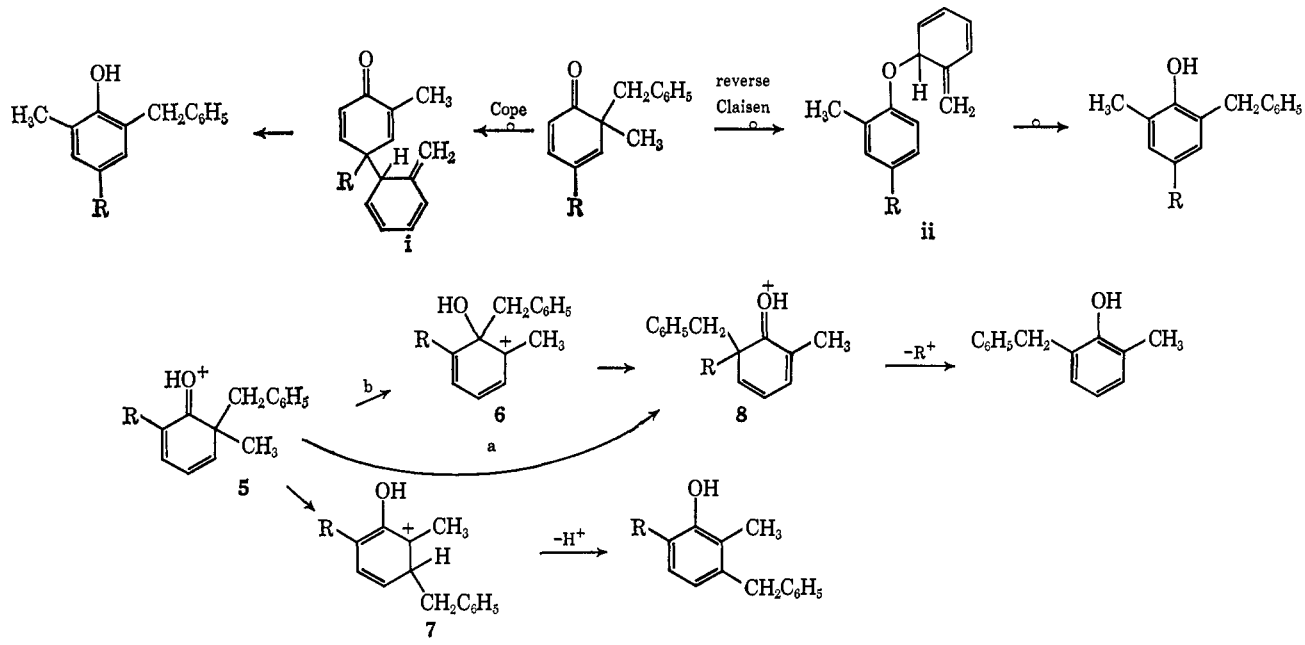

first to the carbonyl carbon and then to C-2 (path b). While these alternatives are quite difficult to distinguish, I believe that the migration of a benzyl group to C-2 in dienone **4** offers significant evidence that a direct [1,5] shift occurs. It has previously been shown that Wagner–Meerwein shifts in the dienone–phenol rearrangement are subject to strong steric inhibition by groups on carbons adjacent to the migration terminus.[1,3c,11] There is no obvious advantage to be gained by migration of a benzyl group to the carbonyl carbon of **4** (rather than to C-5) which would offset the strong steric repulsion by the *t*-butyl group adjacent to the carbonyl. Indeed, even in the absence of any steric considerations, the intermediate carbonium ion **6** should be somewhat less stable than the alternative ion **7** which would result from a shift of the benzyl group to C-5, since **6** lacks the enolic resonance of **7**. A direct [1,5]-sigmatropic shift of the benzyl group, however, would simply convert the protonated ketone **5** to the isomeric protonated ketone **8**. The much greater bond energy of **8**, compared with **7**, should more than compensate for steric compressions in the formation of **8**.

It remains to be explained why the benzyl group in **2** should undergo exclusive [1,5] migration to C-2, while the methyl group in the very similar dienone **1** undergoes exclusive [1,2] migration to C-5. A possible answer lies in the suggestion previously offered to account for the surprising variety and specificity of acid-catalyzed sigmatropic shifts of allyl groups in cyclohexadienones.[1] It was proposed that protonation of the carbonyl group of a cyclohexadienone can take place either on the unbonded (n) electrons or on the π electrons of the carbonyl oxygen. *The nature of the allowed migrations would then be determined by conservation of orbital symmetries*[12] *in these two types of protonated dienones.* According to this concept, the normal[13] n protonation would result in only a slight perturbation of the molecular orbital symmetry pattern of the dienone, and the allowed acid-catalyzed migrations would resemble the allowed thermal migrations in the dienone.[12,14] Since the benzyl group is a good migrator in these reactions, n protonation would be sufficient to cause rearrangement to occur, and thus a thermally allowed [1,5] migration would take place. Poorer migrating groups, such as methyl, would not rearrange in the n-protonated dienone, but would await protonation of the π bond. This would result in conversion of the dienone to a cyclohexadienyl carbonium ion, in which suprafacial [1,2] migrations are allowed, but [1,5] migrations are not.[14–16]

Acknowledgments. I wish to thank the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for grants in support of this work.

(11) P. J. Kropp, *Tetrahedron Lett.*, 1671 (1963).
(12) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968).
(13) G. A. Olah, D. H. O'Brien, and M. Calin, *J. Amer. Chem. Soc.*, **89**, 3582 (1967); G. A. Olah, M. Calin, and D. H. O'Brien, *ibid.*, **89**, 3586 (1967).
(14) H.-J. Hansen and H. Schmid, *Chem. Brit.*, **5**, 111 (1968).
(15) H.-J. Hansen, B. Sutter, and H. Schmid, *Helv. Chim. Acta*, **51**, 828 (1968).
(16) A referee has suggested that the apparent [1,5] migrations may proceed by successive Cope migrations of the benzyl groups to C-4 (forming i) and then to C-2, or by a reverse Claisen rearrangement to oxygen (forming ii) followed by a Cope migration to C-2. The rapid [1,5] migration observed in dienone **3** (R = *t*-Bu), however, clearly does not proceed *via* a Cope migration to C-4. Intermediates such as ii should rearrange rapidly in acid to diphenyl ethers. No such ethers are observed, even when C-2 is blocked by a methyl group. In that case, only [1,2] migration is observed. Finally, it may be noted that [1,5] migrations of benzyl groups are approximately as fast as migrations of allyl groups.[1] Since the reverse Claisen migrations of allyl groups should be some 18 kcal more exothermic than those of benzyl groups, migrations of allyl and benzyl groups by this mechanism should have vastly different rates.

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The Preparation of Alkylmagnesium Fluorides

Sir:

All attempts in the past to prepare and isolate fluoro Grignard compounds have failed.[1] A recent report[2]

(1) (a) H. Gilman, J. Peterson, and F. Schulze, *Rec. Trav. Chim.*, **47**, 19 (1928); (b) G. Schiemann and R. Pillarsky, *Chem. Ber.*, **64**, 134

Table I. Reaction of Hexyl Fluoride with Magnesium in THF[a]

Reaction no.	Mg/RF	Activator or catalyst	Mol % of activator[b]	Time, days	Yield,[c] %	Mg/F ratio of soluble product
1	5.4	None	0	13	0	
2	16.2	BuLi[e]	Trace	9	0	
3	5.4	NaI	4.9	11	0	
4	5.4	$CoCl_2$	2.8	7	0	
				13	52	
				21	95	1.24
5	5.4	Br_2	7	5	73	
6	5.4	I_2	4	6	95	
				14	94	0.94
7[d]	3.2	$BrCH_2CH_2Br$	1.7	3.5	44	
				5.5	73	
				7.5	88	
				14.5	57	
				22.5	42	1.20
8a[d]	5.4	EtBr[e]	2.8	1.5	21	
				4.5	42	
				8.5	51	
				19.5	63	1.11
8b	5.4	EtBr	1	5	0	
				8	36	
				14	87	
				22	94	1.30
8c	5.4	EtBr	27	0.5	41	
				1.0	64	
				1.5	86	
				2.5	91	
				5.0	92	
				8.0	92	1.31
8d	5.4	EtBr	130	0.5	51	
				1.0	77	
				1.5	91	
				2.5	93	
				5.0	94	
				8.0	96	
				14.0	97	1.10
9		None		3	0	
10b		None		6	0	
10c		$CoCl_2$		2.5	3	
				13.5	3	
				36.5	8	

[a] All reactions were carried out under conditions of atmospheric pressure reflux. [b] Based on hexyl fluoride. [c] Based on the formation of hexane by glpc analysis. Toluene used as internal standard in reactions 1, 3, 4, 6, 8b, 8c, and 8d. [d] Magnesium powder was used; other experiments used triply sublimed magnesium turnings. [e] After magnesium was activated, the solution was withdrawn before adding hexyl fluoride.

concerning the possible intermediacy of perfluorophenylmagnesium fluoride prompts us to report results from our laboratory concerning the preparation of the heretofore unknown alkylmagnesium fluorides.

We have prepared for the first time alkylmagnesium fluorides in high yield by the reaction of alkyl fluorides[3]

$$RF + Mg \xrightarrow[\text{catalyst}]{THF} RMgF$$

with magnesium in the presence of appropriate catalysts at reflux temperature in THF. The following facts are most certain evidences for the formation of hexylmagnesium fluoride. First, both the nmr (upfield triplet, δ −0.55, J = 8 cps)[4] and ir spectra (C–Mg stretching, 500 cm^{-1} with shoulder at 548 cm^{-1})[5] of the solutions indicate the formation of the C–Mg bond; second, hexane is formed on hydrolysis of the reaction product; and third, elemental analyses show that the reaction solution contains soluble magnesium and fluoride corresponding to the fluoro Grignard compound.[7]

Reference to Table I shows that hexyl fluoride does not react with magnesium in THF in 13 days under refluxing conditions (reaction 1), even when the mag-

(1931); (c) H. Gilman and L. L. Heck, *J. Amer. Chem. Soc.*, **53**, 377 (1931); (d) J. Bernstein, J. S. Roth, and W. T. Miller, Jr., *ibid.*, **70**, 2310 (1948).

(2) C. Tamborski, G. Moore, and W. L. Respess, 4th International Conference on Organometallic Chemistry, University of Bristol, U. K., July 1969, Abstract C-13.

(3) We have concentrated our attention on the preparation of hexylmagnesium fluoride from hexyl fluoride and magnesium in THF because of the availability and the liquid nature of hexyl fluoride as compared to the gaseous lower alkyl fluorides. Ethylmagnesium fluoride has also been prepared in high yield by this method.

(4) D. F. Evans and J. P. Mayer, *J. Chem. Soc.*, 5125 (1962).

(5) The C–Mg stretching frequency of alkyl Grignard reagents in THF has been cited between 500 and 535 cm^{-1}.[6]

(6) R. M. Salinger and H. S. Mosher, *J. Amer. Chem. Soc.*, **86**, 1782 (1964).

(7) Magnesium was determined by conventional EDTA complexometric titration and by total alkalinity analysis involving acid–base titration.[8] Fluoride analysis was carried out by the method described by Hogan and Tortoric.[9] Other halide ions were determined by potentiometric titration. Magnesium analysis by total alkalinity was always higher than that by EDTA titration. This fact indicates that the hexylmagnesium fluoride prepared from the direct synthesis contains some dialkylmagnesium. This situation also occurs in the preparation of organomagnesium iodides in THF.[6]

(8) H. Gilman, E. Zoellner, and J. Dickey, *J. Amer. Chem. Soc.*, **51**, 1576 (1929).

(9) J. M. Hogan and F. Tortoric, *Anal. Chem.*, **39**, 221 (1967).

nesium was first activated by stirring overnight over BuLi, followed by decantation of the activator before attempting to initiate the reaction (reaction 2). Addition of NaI (reaction 3) or $CoCl_2$ (reaction 4) was also to no avail, except after an induction period of 7 days, when reaction began, using $CoCl_2$ as a catalyst. The reaction is slow; however, the fluoro Grignard was produced in 95% yield after 21 days.

Addition of a catalytic amount of Br_2 (reaction 5), I_2 (reaction 6), ethylene dibromide (reaction 7), and ethyl bromide (reaction 8) also catalyzed the formation of the fluoro Grignard compound. The best results were obtained when I_2 (4%) produced a 95% yield of the fluoro Grignard compound in only 6 days. It is interesting to note that the yield remained constant after an additional 8-day reflux period, whereas when ethylene dibromide and magnesium powder were used, the yield decreased from 88 to 42% during an additional 15-day reflux period. A catalytic amount of ethyl bromide (reaction 8b) produced a high yield (94%) of the fluoro Grignard compound in 22 days. The reaction time can be substantially shortened by addition of larger amounts of ethyl bromide (reactions 8c and d). The latter reactions are essentially entrainment reactions, which have been reported earlier for use in the preparation of chloro, bromo, and iodo Grignard compounds that are difficult to form.[10]

Attempts to prepare alkylmagnesium fluorides by indirect methods have also been attempted. No redistribution occurred when diethylmagnesium was allowed to react with magnesium fluoride (Alfa Inorganics Co.) in Et_2O–THF for 3 days (reaction 9).[11] No metal–halogen exchange took place between diethylmagnesium and hexyl fluoride in Et_2O–THF during 6 days (reaction 10a). However the exchange occurred very slowly in the presence of a catalytic amount of cobalt chloride (reaction 10b).

Both ethyl- and hexylmagnesium fluoride were allowed to react with H_2O, O_2, CO_2, C_6H_5CN, and $(C_6H_5)_2C{=}O$ and the results compared with the results of the same reactions using ethyl- and hexylmagnesium bromide. In all cases the fluoro and bromo Grignard compounds produced the expected product in comparable yields. The fluoro Grignard compounds did react faster than the corresponding bromo compounds toward benzophenone, and gave a higher ratio of addition to reduction.

Studies now in progress involve the extension of the reaction to other alkyl and aryl fluorides and other solvents. Molecular association and nmr studies will be carried out in an attempt to establish the composition of the fluoro Grignard compounds in solution. Work is also in progress to determine the stereoselective nature of the fluoro Grignard compounds as alkylating agents.

Acknowledgment. Partial financial support of this research by the National Science Foundation is gratefully acknowledged.

(10) V. Grignard, *C. R. Acad. Sci., Paris*, **198**, 625 (1935); see M. S. Kharasch and O. Reinmuth, Ed., "Grignard Reactions of Nonmetallic Substances," Prentice-Hall Inc., New York, N. Y., 1954, pp 38–45.

(11) This reaction was previously reported informally by Dessy;[12] however no official report has appeared up to this time. We do not maintain here that magnesium fluoride from some other source will also be inert to redistribution. This possibility is presently being explored.

(12) R. E. Dessy, *Chem. Eng. News*, **38**, (31), 42 (1960).

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Book Reviews

Catalysis in Chemistry and Enzymology. By WILLIAM P. JENCKS, Graduate Department of Biochemistry, Brandeis University, Waltham, Mass. McGraw-Hill Book Co., New York, N. Y. 1969. xvi + 644 pp. 15 × 23 cm.

In the opening chapter of the book Jencks quotes Berzelius who said, "This easy kind of physiological chemistry is created at the writing desk and is the more dangerous, the more genius goes into its execution." After reading Jencks' book a paraphrase of this quotation might be "This sophisticated kind of physical organic chemistry was created at the writing desk and appears more simple, the more genius goes into its elucidation." This 644-page book is a penetrating, scholarly yet readable analysis of the mechanisms underlying enzymatic reactions.

The book as a whole is devoted to the explanation and analysis of those physical organic mechanisms which pertain directly to enzyme catalysis and their application in illustrative enzymatic examples. As a result, solution chemistry is emphasized to the virtual exclusion of gas-phase kinetics, quantum mechanical calculations, and other areas which might be chapters in a more chemically oriented book. Having chosen the subjects which he considers relevant to the enzyme mechanic, Jencks discusses them from the point of view of the physical organic chemist. Yet in the areas chosen he proceeds to the frontiers of present knowledge an maintains the rigor of good physical organic chemistry.

In the first chapter entitled "Approximation," Jencks considers the catalytic consequences of juxtaposition of substrates and catalysts at the surface of an enzyme. This is treated both theoretically and empirically with examples of intramolecular reactions and their relative accelerations compared to intermolecular reactions. Nonenzymatic models in which two molecules are associated by complex formation simulating enzyme–substrate complexes and heterogeneous catalysis are also discussed.

In the second chapter, "Covalent Catalysis" is analyzed. The chapter opens with criteria for the delineation of enzyme–substrate intermediates and the kinetic consequences of such intermediates. It then proceeds to the correlation of structure with nucleophilicity of the attacking atom. Emphasis is on reactions of carbonyl compounds and pyridoxal reactions. The effect of structure on the reactivity of the leaving group is discussed extensively, and the chapter concludes with a brief analysis of oxidative catalysis.

The third chapter deals with general acid and base catalysis. In this chapter the opening pages are largely devoted to model systems. Application to enzymes is exemplified through chymotrypsin and aconitase. The chapter then proceeds to more complex examples and the problems of defining the transition state.