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TITLE: The Energetics of the Combination of a Proton and Hydride Ion

INSTITUTION: University of Cincinnati
Cincinnati, Ohio

INVESTIGATOR: Raymond E. Dessy

GRANT: AF-AFOSR 417-63

FINAL REPORT
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COMPLETED PROJECT SUMMARY

1. Title: The Energetics of the Combination of a Proton and Hydride Ion

2. Principal Investigator: Raymond E. Dessy

3. Junior Research Personnel: Alan Chen

4. Senior Research Personnel:

5. Publications: a) The Ability of "Inert Salts" to Enhance the Rate of Reaction of Grignard Reagents with Unsaturated Linkages, submitted to J. Org. Chem. (attached).

   b) Carbanion Stabilities. Theodore Psarras, R. E. Dessy (in preparation)

6. Abstract of Objectives and Accomplishments:

During the year's extension of our project we have successfully initiated a study into the area of carbanion stabilities - the question of a thermodynamic sequence of stabilities for simple $R:^-$ groups. The first approach has made use of the statistical approach (bags and marbles) in which two metal ions of differing electropositivity are allowed to compete for two groups of differing electronegativity and carbanionic stability.

Nuclear magnetic resonance permits analysis of preferential pairing, and there is reason to believe that the most stable carbanion will prefer at equilibrium to reside on the most electropositive metal. The system

$$Rmg + R'hg \overset{k}{\rightleftarrows} Rhg + R'mg$$

has been examined and Table I reports relative K's for the equilibrium. These are compared with data by Applequist for

$$RLi + \phi I \overset{k}{\rightleftarrows} \phi Li + RI$$

The overlap is inadequate but except for vinyl, the comparison is a good one.

We are extending the series to other groups and comparing the findings with the potential required to affect the second step of the following

$$RHgX \xrightarrow{e} RHg \xrightarrow{e} R:^- + Hg$$

Chart I illustrates the good agreement in sequence between this electrochemical data and the organometallic exchange reactions. With both methods in hand almost any group can be placed in a carbanion stability sequence, just as we have for carbonium ions.

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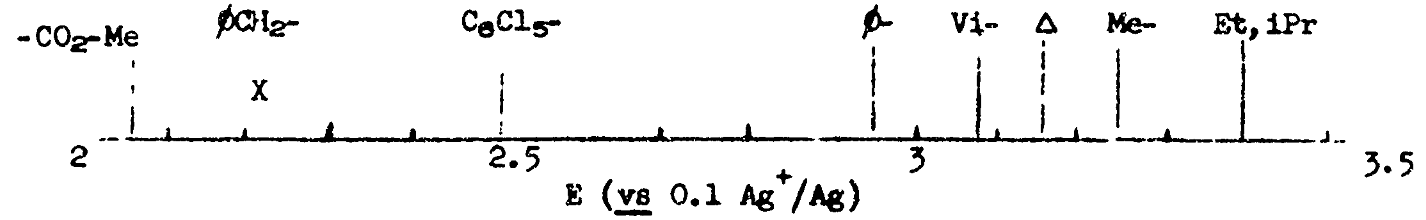
Chart I

RHg $\xrightarrow{e}$



R$_2$Hg $\xrightarrow{2e}$

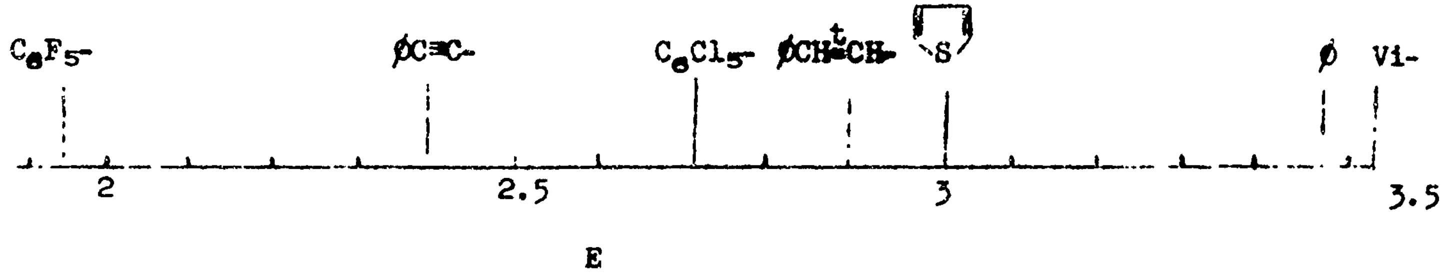


TABLE I

Group	$RLi+\phi I \rightleftarrows$ $\phi Li+RI$	$Rmg+R'hg \rightleftarrows$ $R'mg+Rhg$
i-Pr	--	$\sim 10^{-4}$
Et	$3\cdot10^{-2}$	$\sim 10^{-2}$
CH_3	--	1
cyclo-C_3H_5	10	13
C_2H_3	26,000	30
C_6H_5	100	100
$CH_2=CH-CH_2$	--	170
$C_6H_5CH_2$	--	370

(Applequist & Dessy

Seminars and Speaking Engagements 1963-64

of Raymond E. Dessy[1]

Date	Institution or Organization	City
September 9-13, 1963	Fall Am. Chem. Soc. Meeting	New York, N.Y.
September 26, 1963	University of California, L.A.	Los Angeles, Calif.
October 3, 1963	University of California, LA.	Los Angeles, Calif.
October 30, 1963	Wilmington Delaware, Organic Chemists Club	Wilmington, Dela.
November 15, 1963	Shell Oil Co. Research Laboratories	Oakland, Calif.
November 18, 1963	Stanford, University	Palo Alto, Calif.
December 12, 1963	University of California, Riverside	Riverside, Calif.
January 8, 1964	University of California, Santa Barbara	Santa Barbara, Cal.
January 20, 1964	California Inst. of Technology	Pasadena, Calif.
March 9, 1964	A. C. S. Lima Section	Lima, Ohio
March 10, 1964	A. C. S. Toledo Section	Toledo, Ohio
March 11, 1964	A. C. S. Michigan State Univ. Section	East Lansing, Mich.
March 12, 1964	A. C. S. Univ. of Michigan Section	Ann Arbor, Mich.
March 13, 1964	Polymer Corporation	Sarnia, Ontario
March 13, 1964	A. C. S. Blue Water Section	Port Huron, Mich.
March 16, 1964	A. C. S. Flint Section	Flint, Mich.
March 17, 1964	A. C. S. Grand Rapids Section	Grand Rapids, Mich.
March 18, 1964	A. C. S. South Bend-Elkhart Section	South Bend, Ind.
March 19, 1964	Notre Dame Univ.	South Bend, Ind.
April 3, 1964	Frontiers in Chemistry-Western Reserve	Cleveland, Ohio
April 17, 1964	A. C. S. New Orleans Section	New Orleans, La.
April 29, 1964	Allied Chem. Research Laboratories	Morristown, N.J.
April 30, 1964	Atlantic Refining	Glenolden, Pa.
April 30, 1964	A. C. S. Philadelphia Section	Philadelphia, Pa.
June 9, 1964	Symposium Industrial Syntheses and Applications of Organometallics Sponsored by New York Academy of Sci.	New York, N.Y.
June 22, 1964	Symposium Mechanisms of Inorganic Reactions Sponsored by Inorg. Div. of A. C. S. (Discussion leader only)	Lawrence, Kansas
August 27, 1964	Symposium Reactive Intermediates in Inorganic Chemistry Sponsored by Inorganic Div. of Chemistry Institute of Canada	Quebec City, Canada
September 7-11, 1964	International Conference on Coordination Chemistry Sponsored by IUPAC	Vienna, Austria
September 27, 1964	Lectures Series Chemistry and Properties of Organometallic Compounds Sponsored by Northwestern University	Evanston, Ill.

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[1] On Sabbatical Leave 1963-64

THE ABILITY OF "INERT SALTS" TO ENHANCE THE RATE OF REACTION OF GRIGNARD REAGENTS WITH UNSATURATED LINKAGES, I

Gordon R. Coe, Raymond E. Dessy[1], Stuart I. E. Green
Dept. of Chemistry, University of Cincinnati
Cincinnati 21, Ohio

During an extension of a study dealing with the exchange reaction[2]

$$\underset{1\,M}{R_2\,Mg} + \underset{1\,M}{R_2'\,Hg} \underset{THF}{\rightleftharpoons} R_2'\,Mg + R_2\,Hg$$

it was discovered that the addition of $LiClO_4$ or $(C_4H_9)_4NClO_4$ to the extent of 20 mole % (0.2 M) accelerated the exchange rate so as to reduce the time necessary to reach equilibrium from over thirty hours to less than one hour.

In an effort to utilize this method to increase the rate of reaction of organometals with unsaturated linkages, the system consisting of "BuMgBr" and benzonitrile in ether was chosen as a model because the reaction has been shown to give one product in excellent yields[3] in diethyl ether and the reaction could be conveniently followed experimentally. Lithium perchlorate added to the reaction system produces a rather striking increase

$$\text{"nBuMgBr"} + C_6H_5CN \xrightarrow[Et_2O,\,24^\circ]{LiClO_4} \pm 1^\circ$$

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[1] A. P. Sloan Foundation Fellow.

[2] R. M. Salinger and R. E. Dessy, Tetrahedron Letters, 1963, 729.

[3] C. G. Swain, J. Am. Chem. Soc., 69, 2306 (1947).

in rates of reaction as evidenced by the time required for the mixture to give a negative Gilman test for an organometallic reagent.

To investigate the reaction more thoroughly, a different analytical tool was needed whereby the actual product yields could be determined. The extent of ketimine formation was determined by a modification of the method used by Storfer and Becker[4] in which the ketimine produced was converted upon acid hydrolysis to the ketone which was then precipitated as the 2,4-ditrohydrazone derivative.

Table I shows the yield of ketone (based on "BuMgBr") as a function of inert salt concentration when the reaction was quenched at time, t.

Table I illustrates the increase in yield of ketone as a function of reaction time, and shows that the rate of reaction or effected, but not the extent of reaction.

It should be pointed out particularly that upon the addition of 0.40 F lithium perchlorate, the yield of ketone after twenty five minutes reaction time has been increased from 29.1% without lithium perchlorate to 88.8%.

In an effort to extend the scope of the inert salt effect, other group I salts were considered, but these generally proved to be experimentally undesirable, due to their low solubility or their very hygroscopic nature. Lithium nitrate and lithium-

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[4] S. J. Storfer and E. I. Becker, J. Org. Chem., 27, 1868 (1962).

bromide were tried and proved to enhance the yield of ketone but to a much lesser degree than the perchlorate, probably due to the fact that they did not dissolve completely.

In the reaction of both diethylmagnesium and ethylmagnesium bromide with benzonitrile in tetrahydrofuran[2], the reaction has been found to proceed to only fifty per cent of completion under their reaction conditions. The authors showed that although the remaining fifty per cent of ethyl groups would not react with benzonitrile, when present in equivalent amounts, and was not sufficiently reactive to give a positive Gilman test with Michler's ketone, it was reactive enough to add across benzaldehyde. It was hoped that the yield of ketone could be enhanced upon the addition of inert salt. Butylmagnesium bromide was prepared in THF, and the reaction with benzonitrile followed, both with and without 0.04 F lithium perchlorate. Upon allowing the reactions to proceed for forty eight hours, the yields of ketone in THF, both with and without lithium perchlorate are identical, within experimental error.

Attempts to utilize the method to effect the following reactions failed: $\alpha\text{-NaBr} + \text{BuMgBr} \xrightarrow{\text{Et}_2\text{O}}$; $\text{PhBr} + \text{BuMgBr} \xrightarrow{\text{Et}_2\text{O}}$; $\text{Ph}_2\ \text{C=CH}_2 + \text{BuMgBr} \xrightarrow{\text{Et}_2\text{O}}$; $\text{Ph}_2\ \text{C=CH}_2 + \text{EtMgBr} \xrightarrow{\text{THF}}$; $\text{Et}_3\text{B} + \text{Ph}_2\text{C=O} \xrightarrow{\text{monoglyme}}$: no success in altering the amount of 1,2 vs 1,4 addition of methylmagnesium bromide to isophorone was achieved.

The possible causes of the enhancement in the nitrile case were considered. It is hard to conceive of the lithium perchlorate promoting radical formation as is common in the transition metal salts, but a possible explanation could lie in the formation of an organolithium species through an exchange reaction with the organomagnesium compound, and this new organometal proceeded to react with benzonitrile to produce the ketone upon hydrolysis.

$$\text{"BuMgBr"} + \mathrm{LiClO_4} \rightarrow \mathrm{BuLi} + \mathrm{Mg(Br)ClO_4}$$

$$\mathrm{BuLi} + \mathrm{C_6H_5CN} \rightarrow \text{Product}$$

Disregarding regeneration of the active organolithium compound, this possibility may be excluded by the fact that the addition of only 0.03 and 0.06 mole per cent lithium perchlorate (based on the total amount of magnesium and lithium compounds present) increased the yield of ketone after twenty five minutes from 29.1% to 40.0% and to 55.1% respectively.

To eliminate the possibility of a regenerated organolithium compound as the reacting species, tetrabutylammonium perchlorate was substituted as the inert salt. Once again, an acceleration occurs that is comparable to the lithium perchlorate case. This data is also presented in Table I. This would seem to eliminate the formation of butyllithium as the cause of the enhancement.[5]

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[5] While the reaction of the Grignard reagent with the tetrabutylammonium ion is conceivable, the products would not produce ketone and would therefore lower the yield of ketone. This is found not to be true.

In any case, from a synthetic standpoint, the yields of ketones produced per unit time from the reaction of the Grignard reagent upon nitriles may be appreciably increased upon the addition of either lithium or tetrabutylammonium perchlorate. The use of lithium perchlorate should prove to be the more widely accepted as it is commercially available, inexpensive, and may be dried easily in a pistol at 0.1 mm Hg over refluxing toluene using phorphorous pentoxide.

The accelerated rate of addition of "BuMgBr" to benzonitrile in ether upon the addition of lithium perchlorate is reminiscent of the report of Winstein, Friedrich and Smith[6] on the acceleration of rates of solvolysis of tosylates in ether by lithium salts. Brown and Ichikawa have also reported that the addition of lithium halides to $LiBH_4$ in isopropanol accelerates ketone reductions[7]. Here, ion quadipole interactions were suggested. In the present case, the interaction may involve the substate or the organometal. Infra-red studies on benzonitrile in ether show that lithium perchlorate does not affect carbon-nitrogen triple bond stretching frequency, but such data cannot eliminate substrate-lithium perchlorate quadipole interaction. N.M.R. data on the butylmagnesium bromide - ether system shows that the addition of an equal molar amount of lithium perchlorate has no effect on the spectra obtained but this does not eliminate the possibility of Grignard reagent-lithium perchlorate quadripole interaction.

It is suggested that this system represents, at least in part, another example of the activation of an organometallic

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6. S. Winstein, E.G. Friendrich, and S. Smith, J. Am. Chem. Soc., 86, 305 (1964).

7. H. C. Brown and K. Ichikawa J. Am. Chem. Soc. 83, 4372 (1961).

compound by addition to its environment of "inert salts", similar to the activation of organomercurials and organotins.[8]

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[8] R. E. Dessy and F. Paulik, J. Chem. Ed., 40, 185 (1963), J. Am. Chem. Soc., 85, 1812 (1963); R. E. Dessy, T. Hieber, and F. Paulik, J. Am. Chem. Soc., 86, 28 (1964).

ACKNOWLEDGEMENTS: The authors wish to acknowledge the support and encouragement, in the form of grants, from the Petroleum Research Fund, American Chemical Society PRF-1086 and the Air Force Office of Scientific Research (AFOSR-417-63). One of the authors (G. R. C.) wishes to thank the Gulf Research and Development Co. for support in the form of a fellowship.

TABLE I

$$\text{"nBuMgBr"} + C_6H_5CN \xrightarrow[24^\circ \pm 1^\circ]{Et_2O}$$

0.63M 0.77M

Salt	Salt Conc. (F)	Ave. Per Cent Yield at Time, t[a]			
		5 min.	10 min.	25 min.	44 hrs.
$LiClO_4$	0.00	9.8	16.0	29.1	93.1
$LiClO_4$	0.02			40.0	
$LiClO_4$	0.04	19.7	32.0	55.8	96.0
$LiClO_4$	0.04			88.8	
LiBr	0.04[c]			31.7	94.5
$LiNO_3$	0.04[c]			37.0	89.4
Bu_4NClO_4	0.04			55.1	
$LiClO_4$[b]	0.00				60.3
$LiClO_4$[b]	0.04				57.3

[a] Ave. per cent yield based on at least two samples in each case.

[b] THF solvent rather than Et_2O.

[c] Salts only partially dissolved.