[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Relative Reactivities of Organolithium and Organomagnesium Compounds

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Introduction

The color test for reactive organometallic compounds provides a means for measuring the relative reactivities of such compounds. It has been used for determining the reaction rates of various Grignard reagents with selected reactants[1a,b,c] and for distinguishing between RMgX and R_2Mg compounds.[1d] The present work, a continuation of studies on the relative reactivities of organometallic compounds, compares *n*-butyl- and phenyl-lithium with *n*-butyl- and phenylmagnesium bromides. On the basis of a series of typical reactants, there is no doubt concerning the greater reaction velocities of organolithium compounds. It has been shown recently that organolithium compounds react more rapidly than RMgX compounds with secondary amines.[2] Where comparisons can be made from the present results it is generally true that *n*-butyl-lithium undergoes more ready reaction than phenyl-lithium. This also is in agreement with observations like the more rapid addition of *n*-butyl-lithium, when compared with phenyl-lithium, to 1,1-diphenylethylene.[3] It would be ill-advised, in view of related studies with organomagnesium halides, to make sweeping generalizations to the effect that all organolithium compounds are more reactive than the corresponding Grignard reagents, and that all alkyl-lithium compounds react more rapidly than aryl-lithium compounds.

It may be held that it is unwarranted to draw conclusions on the relative reactivities of organolithium and organomagnesium compounds when the types studied are different. That is, a comparison of phenyl-lithium with diphenylmagnesium might properly be considered more fair than a comparison of phenyl-lithium with phenylmagnesium bromide. However, the present available evidence shows that RMgX compounds react more rapidly than the corresponding R_2Mg compounds.[1d,e] It now appears generally true that the following is the order of decreasing activity of some highly active organometallic compounds: Cs, Rb, K, Na, Li, Mg.

Compounds which React with Organolithium but Not with Organomagnesium Types.—There are occasional functional groups which undergo reaction with organolithium compounds but not with the Grignard reagent. The outstanding illustration is the olefinic linkage in some hydrocarbons. It has been rather thoroughly demonstrated that the Grignard

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[1] (a) Gilman and Pickens, THIS JOURNAL, **47**, 2406 (1925); (b) Gilman, Heck and St. John, *Rec. trav. chim.*, **49**, 212 (1930); (c) Gilman and St. John, *ibid.*, **49**, 222 (1930); (d) Gilman and Brown, THIS JOURNAL, **52**, 1181 (1930); (e) Bachmann, *ibid.*, **52**, 4412 (1930).

[2] Ziegler and Ohlinger, *Ann.*, **495**, 84 (1932).

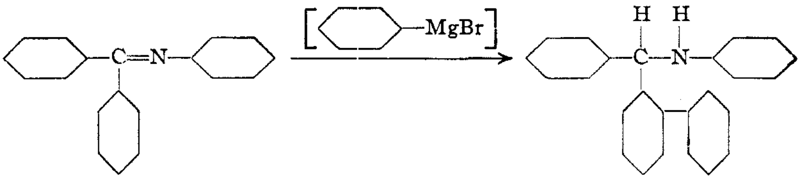
[3] Ziegler and Colonius, *ibid.*, **479**, 135 (1930).

reagent does not add, in the numerous cases so far investigated, to a simple olefinic linkage. Admittedly, the apparent absence of reaction may merely be a limiting case of an extremely slow reaction.

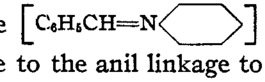
Actually, the only important functional groups or linkages which do not undergo reaction with RMgX compounds are the olefinic and acetylenic (disubstituted) linkages. Practically all other functional groups enter into reaction with Grignard reagents. However, occasional members of a given series appear not to react with organomagnesium halides. The present striking illustrations are nitriles. *p*-Dimethylaminobenzonitrile has been recovered unchanged after attempted reaction with ethylmagnesium iodide and phenylmagnesium bromide;[4] and *p*-methoxybenzonitrile was observed not to undergo reaction with Grignard reagents under conditions that induced reaction with benzonitrile.[5] We have shown that each of these ketones reacts quite promptly with both methyl- and phenyl-lithium to give the normal and expected ketonic products.

Different Types of Reaction of Organolithium and Organomagnesium Compounds with a Selected Reactant.—Partly because of the different reactivities of organolithium and organomagnesium compounds it might be expected that some compounds, especially those with poly-functional groups, will undergo distinctive and different reactions with corresponding members of these organometallic types. Reactions of this kind have been observed, and are now reported, with benzophenone-anil [$(C_6H_5)_2C=NC_6H_5$].

Benzophenone-anil reacts decidedly slowly, if at all, when refluxed with phenylmagnesium bromide in ether.[6] However, when the ether is largely replaced by toluene and the mixture refluxed for ten hours at 90–105°, a highly unusual reaction takes place leading to the formation of *o*-phenylbenzohydrylaniline.



(I)

This secondary amine owes its formation to the unique 1,4-addition to a conjugated system which is partly lateral and partly nuclear. Apparently, the forced conditions of reaction are necessary to overcome steric hindrance inasmuch as benzal-aniline  undergoes addition with phenylmagnesium bromide to the anil linkage to give benzohydrylaniline.

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[4] Sachs and Sachs, *Ber.*, **37**, 3089 (1904).

[5] Angeli, *Atti. accad. Lincei*, [6] **3**, 450 (1926) [*Chem. Abstracts*, **20**, 2843 (1926)]. See also Angeli, "Sammlung chemischer und chemisch-technischer Vorträge," **28–29**, 30 (1924–27).

[6] Gilman, Kirby and Kinney, THIS JOURNAL, **51**, 2252 (1929).

A similar reaction involving 1,4-addition to a nuclear-lateral conjugated system has been observed with highly phenylated ketones.[7]

Phenyl-lithium does react with benzophenone-anil in *ether* and the product obtained is triphenylmethylaniline.

$$(C_6H_5)_2C{=}NC_6H_5 + C_6H_5Li \longrightarrow (C_6H_5)_3CNHC_6H_5 \qquad \text{(II)}$$

This simple addition to the anil linkage in benzophenone-anil has not so far been observed with phenylmagnesium bromide. Furthermore, when the reaction is forced by refluxing an ether–toluene mixture of the anil with phenyl-lithium, the reaction mixture yields triphenylmethylaniline. So far none of the *o*-phenylbenzohydrylaniline (I) has been isolated.

It appears reasonable to attribute the different reactions with phenylmagnesium bromide to steric influences, not alone of the benzophenone-anil but also of the Grignard reagent. For example, the Grignard reagent is an equilibrium mixture containing, in part,[8] the following components.

$$2C_6H_5MgBr \rightleftharpoons (C_6H_5)_2Mg + MgBr_2 \qquad \text{(III)}$$

If diphenylmagnesium is the more effective reactant with the anil, then it might be expected that its greater molecular volume, when compared with the simpler phenyl-lithium, would significantly increase the already marked steric effects of the phenyl groups accumulated about the anil linkage in benzophenone-anil. This remains to be determined with related compounds. For the present, it may serve as a working basis to interpret different reactions of these, and other, organometallic compounds in reactions with compounds like naphthalic anhydride.[9] This would hardly serve as a sole explanation, for we are undoubtedly concerned with essential differences in reactivity independent of steric effects.

Just prior to the receipt of proof, an article [Bergmann and Rosenthal, *J. prakt. Chem.*, **135**, 267 (1932)] appeared describing the formation of *o*-phenylbenzohydrylaniline from the interaction of benzophenone-anil and phenyl-lithium. It is quite probable that their product (m. p. 144°) was triphenylmethylaniline (m. p. 147°) and not *o*-phenylbenzohydrylaniline (m. p. 144°). The hydrochloride obtained by them melted at 186°, whereas the hydrochloride of *o*-phenylbenzohydrylaniline[6] melts at 182.5°. The mistaken identity is somewhat understandable in view of the related melting points.

Experimental Part

The general procedures were those employed previously with Grignard reaction rate studies.[1b,6] All reactions were effected in a nitrogen atmosphere, and during refluxing the solutions were maintained under a slight positive pressure exerted by nitro-

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(7) Kohler and Nygaard, THIS JOURNAL, **52**, 4128 (1930). See also Kohler and Baltzly, *ibid.*, **54**, 4015 (1932).

(8) Gilman and Fothergill, *ibid.*, **51**, 3149 (1929).

(9) Wittig, Leo and Wiemer, *Ber.*, **64**, 2405 (1931). For other illustrations of different reactions see Ziegler and Zeiser, *ibid.*, **63B**, 1847 (1930); *Ann.*, **485**, 174 (1931); Bergmann, Blum-Bergmann and von Christiani, *ibid.*, **483**, 80 (1930).

gen and controlled by a mercury trap. The ether used throughout the experiments was freshly distilled under anhydrous conditions from a solution of phenylmagnesium bromide. A 10% excess of reactant was used. The times were recorded when one-half of the organometallic compound had been added (in some cases the addition cannot be made rapidly because of the violent refluxing of the ether) and to a negative color test[10] with a 10-cc. portion of the reaction mixture.

In experiments with *n*-butyl-lithium, 20 cc. of 1 *N* solution (0.02 mole) was added to the reactant in 90 cc. of ether. In all other cases 15 cc. of a 1.33 *N* solution of organometallic compound was added to the reactant in 95 cc. of ether. The effect of concentration on reaction velocities has been examined,[10] and the slight change in concentration during the addition of *n*-butyl-lithium is not significant because an immediate reaction was observed with this compound. Inasmuch as *n*-butyl-lithium reacts with ether at a moderate rate, it was used directly after its preparation. Apropos of the stability of *n*-butyl-lithium, it is interesting to note that in a blank qualitative experiment, 0.02 mole in 110 cc. of ether was refluxed for four hours, then allowed to stand for fifteen hours and finally refluxed for eight hours to yield a solution such that one cc. gave a strong color test. After setting aside this solution for three weeks a 1-cc. sample gave a negative color test, but a 10-cc. sample gave a fairly strong color test. At the end of four weeks, a 10-cc. sample gave a negative test.

Earlier rate studies with some RMgX compounds were confirmed. The present results, given in Table I, were obtained with different concentrations than those used previously. Preliminary experiments having shown the marked differences in reaction velocities, the first samples were generally removed after an elapsed time of four minutes. The maximum times given with the less reactive RMgX compounds as 8+ hours means simply that the time required for complete reaction is in excess of eight hours and not necessarily between eight and nine hours.

Miscellaneous Rate Observations.—In order to determine the effect of long-chained organometallic compounds on relative reactivities, *n*-lauryl-lithium (*n*-$C_{12}H_{25}Li$)[11] was compared with *n*-laurylmagnesium bromide in reactions with benzonitrile. After refluxing a solution of 0.03 mole of *n*-lauryl-lithium with 0.033 mole of benzonitrile in a total ether volume of 220 cc. for four minutes, a negative color test was observed. Under corresponding conditions, *n*-laurylmagnesium bromide gave a strong positive test after refluxing for three hours. In both cases the solutions were clear yellow in color and free of precipitate. Accordingly, the length of the carbon chain is without essential influence on the relative rates of reaction of the two types of compounds.

Nitrobenzene and benzophenone are known to react promptly with phenylmagnesium bromide. They react at once with phenyl-lithium, the former giving a black reaction mixture and the latter a white precipitate. *n*-Butylmagnesium bromide reacts at once with ethyl cinnamate in a (0.02:0.011) ratio, and at once with nitro-*p*-xylene in a (0.02:0.0067) ratio.

The only anomalous compound so far encountered is *n*-valeronitrile. With 0.022 mole of this nitrile and 0.02 mole of either phenylmagnesium bromide or phenyl-lithium the time is 6+ hours. However, with 0.044 mole of the nitrile and 0.02 mole of either phenylmagnesium bromide or phenyl-lithium the time is eight minutes. The absence of significant time differences with essentially equimolecular proportions of reactants warrants a further study of nitriles.

Reaction between Nitriles and Organolithium Compounds.—To 3.21 g. (0.022 mole) of *p*-dimethylaminobenzonitrile in 56.5 cc. of ether was added 0.02 mole of methyl-lithium in 53.5 cc. of ether. The color test at the end of four minutes was negative.

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[10] THIS JOURNAL, **47**, 2002 (1925).

[11] The authors are grateful to Mr. E. A. Zoellner for this organolithium compound and for other assistance.

TABLE I

REACTIONS WITH C_6H_5MgBr, C_6H_5Li, n-C_4H_9MgBr AND n-C_4H_9Li

				0.02 Mole C_6H_5MgBr			0.02 Mole C_6H_5Li		
					Appearance			Appearance	
No.	Reagent	G.	Mole	Time, hours	Soln.	Ppt.	Time, hours	Soln.	Ppt.
1	C_6H_5CN	2.27	0.022	1.3	Colorless	White	0.07 −	Red	None[a]
2	$C_6H_5CH_2Cl$	2.78	.022	8+	Colorless	None	2.4	Colorless	White
3	$C_6H_5N{=}NC_6H_5$	4.00	.022	8+	Red	Yellow	0.07 −	Green	Black[b]
4	$(C_2H_5)_2SO_4$	3.39	.022	8+	Colorless	White	.23	Colorless	White
5	$C_6H_5CH{=}NC_6H_5$	3.98	.022	8+	Yellow	None	.07	Yellow	None[c]
6	$(C_6H_5)_2C{=}NC_6H_5$	5.65	.022	8+	Yellow	None	7 ± 1	Green	Black
7	$C_6H_5CH{=}CHCO_2C_2H_5$	1.94	.011	1.6	Yellow	None	0.07 −	Yellow	White
8	1,2,4-$C_6H_3(CH_3)(NO_2)$-(CH_3)	1.113	.0067	1.3	Red	None	.07 −	Red	None
9	Furfural	2.11	.022	0.07 −	Yellow	White	.07 −	Yellow	None
10	$(CH_3)_3CCOCH_3$	2.20	.022	0.07 −	Colorless	None	.07 −	Yellow	None

				0.02 Mole n-C_4H_9MgBr			0.02 Mole n-C_4H_9Li		
					Appearance			Appearance	
No.	Reagent	G.	Mole	Time, hours	Soln.	Ppt.	Time, hours	Soln.	Ppt.
1	C_6H_5CN	2.27	0.022	8+	Yellow	White	0.07 −	Orange	None
2	$C_6H_5CH_2Cl$	2.78	.022	8+	Colorless	None	.07 −	Colorless	White
3	$C_6H_5N{=}NC_6H_5$	4.00	.022	0.5	Red	Yellow	.07 −	Green	Black
4	$(C_2H_5)_2SO_4$	3.39	.022	8+	Colorless	White	.11	Colorless	White
5	$C_6H_5CH{=}NC_6H_5$	3.98	.022	8+	Yellow	None	.07 −	Yellow	None

[a] The yield of benzophenone was 60%.

[b] When 0.011 mole of azobenzene was refluxed with 0.02 mole of phenyl-lithium, a negative color test was not obtained after several hours. The proposed mechanism for this reaction is incomplete and is being investigated further.

[c] The yield of benzohydrylaniline was 67%. It was identified by a mixed melting point determination of its hydrochloride.

The excess nitrile was then removed by the addition of 0.004 mole of methyl-lithium. The yield of *p*-dimethylaminoacetophenone was 45%. A corresponding reaction between 0.011 mole of *p*-dimethylaminobenzonitrile and phenyl-lithium also took place promptly (no color test in four minutes), to yield 56% of *p*-dimethylaminobenzophenone. Identification of this ketone was supplemented by the preparation of its oxime.

To 2.93 g. (0.022 mole) of *p*-methoxybenzonitrile in 56.5 cc. of ether was added 0.02 mole of methyl-lithium in 53.5 cc. of ether, and a negative color test was observed after four minutes. The yield of *p*-methoxyacetophenone was 75%. In a corresponding reaction with 2.93 g. (0.022 mole) of *p*-methoxybenzonitrile in 90 cc. of ether and 0.02 mole of phenyl-lithium, the negative color test was observed at the end of thirty minutes; the yield of *p*-methoxybenzophenone was 85%; and characterization was completed by the preparation of the oxime.

Benzophenone-anil and Phenyl-lithium.—To 25.7 g. (0.1 mole) of benzophenone-anil in 120 cc. of ether was added 0.1 mole of phenyl-lithium in 80 cc. of ether. The greenish-black reaction mixture was refluxed for six hours, and then worked up in a customary manner to yield 71% of triphenylmethylaniline which was identified by the method of mixed melting points. In another experiment, the product obtained by refluxing 0.45 mole of benzophenone-anil with 0.05 mole of phenyl-lithium in an ether-toluene mixture for one hour at 95° was triphenylmethylaniline in a 68% yield. The reactants in this latter experiment were mixed at about 95°.

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Summary

1. A study of the relative reactivities of organolithium and organomagnesium compounds shows that the former undergo more rapid reaction with a selected number of typical reactants. Also, *n*-butyl-lithium is more reactive than phenyl-lithium.

2. Some compounds, like *p*-dimethylaminobenzonitrile and *p*-methoxybenzonitrile, which do not react with the Grignard reagent, undergo prompt reaction with methyl- and phenyl-lithium to give the expected products.

3. The unusual 1,4-addition of phenylmagnesium bromide to the lateral-nuclear conjugated system in benzophenone-anil is not shown by phenyl-lithium which adds normally to the anil linkage, both under mild and forced conditions, to give triphenylmethylaniline. An explanation based, in part, on the different molecular volumes of the two organometallic compounds is proposed to account for the differences in behavior with sterically hindered functional groups.

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