ELECTRONIC EFFECTS IN ORGANOMAGNESIUM REACTIONS[1,2]

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ABSTRACT

The kinetics of the first part of the reaction between para-substituted benzonitriles and diethylmagnesium have been studied. The rarely isolated intermediate products, the ketimines, have been isolated and identified. The kinetic constants fit a Hammett plot, with rho equal to +1.57.

Recently, a precise, convenient procedure was reported for following kinetics of the Grignard reaction (1). The purpose of this investigation was to use this method in evaluating the electronic effect of *p*-substituents in the reactions between the substituted benzonitriles and diethylmagnesium.

EXPERIMENTAL

Reagents

The magnesium used has been previously described (1). All other reagents for kinetics, with the exceptions noted below, were purified in the usual manner. Diethylmagnesium in tetrahydrofuran was prepared by the method of Storfer and Becker (1). The solutions were colorless and were standarized by the method of Gilman *et al.* (2). No precipitate was observed when test portions of the diethylmagnesium solutions (approximately 0.5 to 1 ml) were hydrolyzed in acidified silver nitrate solution. All work with organomagnesium compounds was carried out in an atmosphere of either nitrogen or argon.

α,α,α-Trifluoro-p-tolunitrile

A solution of α,α,α-trifluoro-*p*-tolylmagnesium bromide was prepared in the usual manner from 40 g (0.18 mole) of α,α,α-trifluoro-*p*-bromotoluene in 175 ml anhydrous ether. The Grignard solution was then filtered through a glass-wool plug into an addition funnel.

In a 500-ml flask equipped with stirrer, gas inlet tube, and condenser was placed 125 ml of anhydrous ether. Twelve grams (0.20 mole) of cyanogen chloride (3) were distilled into the flask. The cyanogen chloride solution was cooled in an ice bath and the Grignard solution added over a period of 2.5 hours. After standing overnight, the mixture, which had separated into two layers, was hydrolyzed with cracked ice and then dilute sulphuric acid. The ether layer was dried with anhydrous sodium sulphate, distilled on a steam bath, and the residue was then vacuum distilled, yielding two fractions: the first, 10.1 g, boiling from 35 to 58° at 6 mm; the second, 6.1 g, boiling from 58 to 62° at 5.5–6.0 mm (total 16.2 g, 0.094 mole, 52.5%). The higher-boiling fraction was then purified for analysis by three-stage fractional freezing and one crystalization from pentane, m.p. 36.4–37.4° (reported (4) 36–37°). The total yield of purified nitrile was 5.9 g (0.035 mole, 19.1%). Anal. Calc. for $C_8H_4F_3N$: C, 56.15; H, 2.36; N, 8.19. Found: C, 56.07; H, 2.60; N, 8.10.

4′-(Trifluoromethyl)-propiophenone

The title compound was made via bis(α,α,α-trifluoro-*p*-tolyl)cadmium by the method of Gilman and Nelson (5). The organocadmium was prepared through the corresponding Grignard reagent using 10 g (0.044 mole) α,α,α-trifluoro-*p*-bromotoluene and 4.5 g (0.025 mole) cadmium chloride. The mixture was then treated with 3.8 ml (0.044 mole) propionyl chloride. After hydrolysis, the organic layer was concentrated on a steam bath and the residue extracted with Girards "T" reagent. After hydrolyzing the Girard derivative with hydrochloric acid, and extracting the ketone with ether, 1.25 g (0.0057 mole, 12.9%) of a solid, m.p. 35.6–36.8°, was obtained. The ketone was crystallized twice from pentane and once from ethanol–water, m.p. 35.6–37.0°. Anal. Calc. for $C_{10}H_9F_3O$: C, 59.41; H, 4.49. Found: C, 59.45; H, 4.58.

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[2] *Taken in part from the thesis submitted by J. D. Citron to the Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Bachelor of Science in Chemistry, June 1962.*

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Method of Analysis

This method is based upon that described in reference 1. An aliquot of the solution under study was hydrolyzed in a known excess of sulphuric acid (10.00 ml of 0.06–0.10 *N*) containing ethanol (about 10 ml) to dissolve the organic materials present. The solution was heated to just below the boiling point for 15 minutes to dissolve the magnesium compounds present, and was then back-titrated while hot with sodium hydroxide solution (0.04–0.06 *N*) to the methyl red end point.

Blanks were run to determine whether the organic species present affected the results. Approximately 0.1–0.2 g each of nitrile and substituted propiophenone were added to a mixture of 5 ml sulphuric acid and 5 ml ethanol. After heating to just below the boiling point for 15 minutes, the solutions were back-titrated while hot using methyl red indicator. The results were the same within experimental error as a blank using only sulphuric acid.

Kinetics

The apparatus and reaction conditions have been previously described (1). Before starting a run, a measured volume of a standardized solution of diethylmagnesium in tetrahydrofuran was introduced into the reaction vessel. At time zero, a thermostatted standard solution of the nitrile in tetrahydrofuran was introduced into the diethylmagnesium solution. At appropriate intervals, samples were withdrawn by syringe for analysis. All solutions remained homogeneous during and after the kinetic runs. The ratios of nitrile to diethylmagnesium ranged from 1:1 to 2.5:1, and the concentration of diethylmagnesium ranged from 0.10 to 0.22 *M*.

Reaction Products

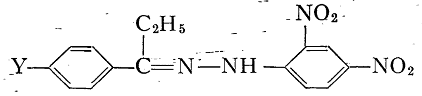
(1) 2,4,6-Tris-(*p*-chlorophenyl)-*s*-triazine was isolated in preliminary runs with *p*-chlorobenzonitrile when the nitrile:Et_2Mg ratio exceeded 2:1. At 30° in tetrahydrofuran, with a 3:1 ratio, a precipitate, the triazine, appeared after 24 hours, m.p. 332.0–332.9°. It was identified by elemental analysis, mixed melting point, 332.3–333.2°, with an authentic sample, m.p. 332.6–333.6° (reported (6) 335°), and identity of their infrared spectra. The triazine was very insoluble in tetrahydrofuran at 30°.

An attempt was made to increase the yield of triazine. Twenty-five milliliters of a 0.5 *M* Et_2Mg (0.0125 mole) solution in tetrahydrofuran and 5.0 g (0.0445 mole) *p*-chlorobenzonitrile were refluxed for 3 days. A precipitate appeared after the first 24 hours. A mixture of 20 ml of water and 5 ml of concentrated hydrochloric acid was added, filtration affording 1.49 g (45.6% theoretical, after subtracting the amount of nitrile consumed in ketimine formation) of crude triazine.

(2) 2,4-Dinitrophenylhydrazone derivatives of *p*-substituted propiophenones were prepared by adding the ketone to an excess of a stock solution (1) of 2,4-dinitrophenylhydrazine and recrystallizing the precipitates. The data are summarized in Table I.

TABLE I

2,4-Dinitrophenylhydrazones of *p*-substituted propiophenones



Y	Yield, %*	Melting point, °C	Empirical formula	Analyses, %					
				C		H		N	
				Calc.	Found	Calc.	Found	Calc.	Found
CF_3	44, orange	188.9–190.3†	$C_{16}H_{13}F_3N_4O_4$	50.27	50.32	3.43	3.72	14.66	14.65
Cl	95, orange	219.6–220.5‡	$C_{15}H_{13}ClN_4O_4$§	51.65	51.68	3.76	3.64	16.07	16.12
C_6H_5	97, orange-red	216.5–218.5‖	$C_{21}H_{18}N_4O_4$	64.61	64.90	4.65	4.94	14.35	14.54
		(decomp.)			64.85		4.78		14.32
CH_3	44, red	200.0–205.5¶							
OCH_3	64, deep red	194.0–197.2**							

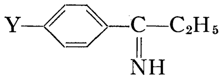
*Starting with 120 mg of ketone in each case. Yields are after one recrystallization; melting points are uncorrected.
†Recrystallized from ethanol, chloroform–methanol, and ethanol – ethyl acetate.
‡Recrystallized twice from ethanol – ethyl acetate and twice from ethanol.
§Calc.: Cl, 10.17. Found: Cl, 9.99.
‖Recrystallized twice from ethanol – ethyl acetate and twice from chloroform–methanol.
¶Reported m.p. 200–202° (L. M. Long and H. R. Henze. J. Am. Chem. Soc. **63**, 1939 (1941)).
**Reported m.p. 195° (N. M. Cullinane, S. J. Chard, and D. M. Leyshon. J. Chem. Soc. 376 (1952)).

Ketimines

The method used was that of Pickard and Tolbert (7). Ethylmagnesium bromide was employed with the nitrile in ether. The imines were handled under anhydrous conditions at all times, as they appeared to be very sensitive to hydrolysis. The physical constants will be found in Table II.

TABLE II

p-Substituted phenyl ethyl ketimines



				Analyses, %					
				C		H		N	
Y	Color	Boiling point, °C (mm of Hg)*	Empirical formula	Calc.	Found	Calc.	Found	Calc.	Found
Cl	Yellow liquid	115 (4.4)	$C_9H_{10}ClN$†	64.48	64.60	6.01	5.81	8.36	8.58
C_6H_5	White solid	84.0–87.0‡	$C_{15}H_{15}N$	86.08	86.08	7.22	7.40	6.69	6.95
CH_3	Yellow liquid	101–105 (4.5)	$C_{10}H_{13}N$	81.58	81.72	8.90	9.15	9.52	9.40
OCH_3	White solid	128 (4.7)§	$C_{10}H_{13}NO$	73.59	73.58	8.03	7.99	8.58	8.78

*Block temperature of a molecular still.
†Calc.: Cl, 21.15. Found: Cl, 21.19.
‡Melting point.
§M.p. 46.7–48.6°. Reported m.p. 38–40° (P. L. Couturier. Ann. Chim. **10**, 559 (1938)).

RESULTS

The initial concentration of nitrile was calculated from the number of moles added and the initial volume of the reaction mixture. The initial concentration of diethylmagnesium was obtained by the above method, or by extrapolating the early points (less than 10% reaction) back to zero time; the agreement between the two methods was an internal check on the technique for each run (see reference 1).

A second-order rate equation, first order in diethylmagnesium and first order in nitrile, gave consistent values for the rate constant (eq. [1]). The rates thus obtained are shown in Table III, together with the appropriate data for the Hammett plot. The Hammett plot is given in Fig. 1, and the ρ is +1.57. The Hammett plot and all kinetic curves were fitted by the method of least squares.

$$[1] \qquad \text{rate} = k[Et_2Mg][\text{nitrile}]$$

TABLE III

Kinetic data

Y	*k**	Number of runs	log k/k_0	sigma†
CF_3	23.8 ±0.0	2	0.848	0.550
Cl	7.47±0.10	2	0.344	0.227
C_6H_5	3.65±0.22	5	0.033	0.009
H	3.38‡		0.000	0.000
CH_3	1.60±0.10	5	−0.325	−0.170
OCH_3	1.30±0.00	2	−0.415	−0.268

*In liter/mole-sec×10^4; ± values are average deviations from the mean.
†See ref. 8.
‡Rate constant from ref. 1.

DISCUSSION

The precision of the analytical procedure made possible the study of the initial rates of the reaction. This point is significant, since it was shown earlier (1) that only half of the available ethyl groups react, and that for this half two reaction rates are observed. It is within the time for reaction of this first quarter of the available ethyl groups that the data were obtained in the present work.

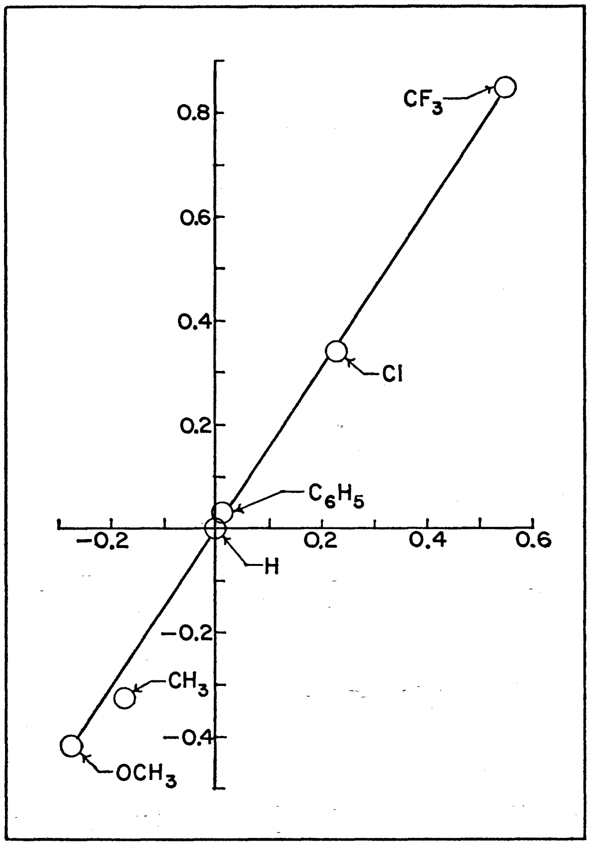
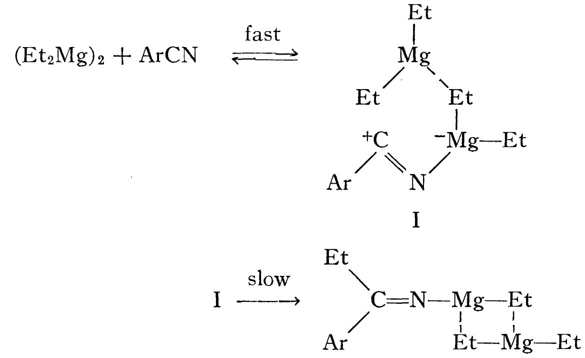


FIG. 1. Hammett plot of reaction rate constants. Slope (ρ) = +1.57. Ordinate: log (k/k_0); abscissa: σ.

The linearity of the Hammett plot affirms that the nitriles taken here react by the same mechanism. The value of ρ, +1.57, indicates that the rate-determining step involves a dipolar, but probably not ionic, species as befits a solvent of low dielectric constant such as tetrahydrofuran.

The mechanism previously proposed (1) for the first part of the reaction can be used to explain the electronic effects of the substituents. The role of the solvent is not considered in this mechanism. The increased rate with the electron-attracting chlorine atom in the



para position is consistent with the rearrangement of the complex as the slow step, since that step requires the transfer of a negative ethyl group to an electron-deficient center—the nitrile carbon atom. Conversely, electron-releasing groups, such as CH_3 and OCH_3, should decrease the rate by increasing the electron density at the nitrile carbon atom, making the transfer of a negative ethyl group there more difficult, which is the case.

Prior workers in this area of research have employed competition experiments and found the effect of substituents to be in qualitative agreement with the results obtained here. Thus, Gilman and Lichtenwalter (9) found the order of reactivities to be $Cl > H > CH_3 > OCH_3 > N(CH_3)_2$ for the reaction between phenylmagnesium bromide and the *p*-substituted benzonitriles in ethyl ether. In a study of the competitive reaction between *p*-substituted benzophenones and 1-naphthol against methylmagnesium iodide in phenetole, Lewis and Wright (10) obtained a ρ of $+0.362$.

The appreciable changes in the rate with changes in substituent obtained in the reactions with benzonitriles appear to be significantly different from those reported by Dessy and Salinger (11) for the reaction of *p*-substituted benzalanilines with ethylmagnesium bromide in ethyl ether. In that study the authors claim that essentially no change in rate is observed with the methoxy or chloro groups.

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