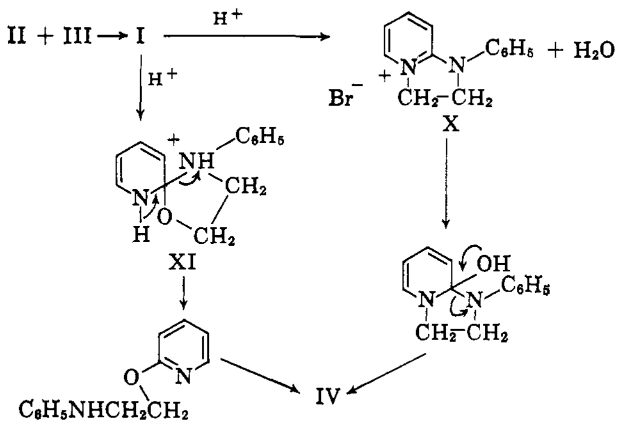


Experimental[7]

Preparation of N-(β-Anilinoethyl)-2-pyridone (IV).—A mixture of 47.4 g. (0.3 mole) of 2-bromopyridine and 82.2 g. (0.6 mole) of N-phenylethanolamine were heated at reflux for 6 hr. The solution was diluted with water and extracted with chloroform; the aqueous layer (pH 6) was made alkaline with 50% sodium hydroxide solution. The brown oil which separated solidified on standing. Two recrystallizations from carbon tetrachloride provided 26.8 g. (41.5%) of IV as the one-half hydrate, m.p. 109.5–110°.

Anal. Calcd. for $C_{13}H_{14}N_2O\cdot0.5H_2O$: C, 69.92; H, 6.77; N, 12.55. Found: C, 69.97; H, 6.49; N, 12.55.

A 2.0-g. sample of IV was refluxed for 39 hr. in benzene under a Dean–Stark trap. Anhydrous IV was obtained as white needles, m.p. 108–109°.

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.58; N, 13.08. Found: C, 72.82; H, 6.58; N, 13.13.

The infrared spectrum of anhydrous IV exhibited peaks at 1653, 3340, 1513, and 1256 cm.$^{-1}$. The ultraviolet spectrum in ethanol exhibited absorption maxima at 298 mμ (ε 2375), 247 (4575), and 237 (4280). Similar spectra have been observed for other 2-pyridones.[8]

Treatment of IV with phenyl isothiocyanate and recrystallization of the resulting solid from carbon tetrachloride provided the phenylthiourea derivative of IV, m.p. 144–146°.

Anal. Calcd. for $C_{20}H_{19}N_3OS$: C, 68.74; H, 5.48; N, 12.03. Found: C, 68.61; H, 5.37; N, 12.10.

Hofmann Degradation of IV.—To 1.30 g. (0.006 mole) of IV in 25 ml. of ethanol was added 1.7 g. (0.012 mole) of potassium carbonate and 2.56 g. (0.018 mole) of methyl iodide. The mixture was refluxed for 31 hr. and additional potassium carbonate and methyl iodide were occasionally added. The reaction mixture was filtered and evaporated to provide the yellow quaternary salt.

The salt was dissolved in water and treated with 5.0 g. of silver oxide. The solution was stirred for 1 hr., filtered, and slowly distilled. The distillate was extracted with ether to provide 0.6 g. of N,N-dimethylaniline: b.p. 193.9°, $n^{20}D$ 1.5583; lit.[9] b.p. 192.5–193.5, $n^{20}D$ 1.5582. The infrared spectrum of the compound was identical with that of authentic N,N-dimethylaniline. The distillation residue was extracted with ether. Removal of the solvent provided an oil which crystallized to yield 0.9 g. of V, m.p. 118–121°. Sublimation raised the melting point to 121–123°, lit.[10] m.p. 119–122°. The mercury(II) chloride salt melted at 193–195°, lit.[10] m.p. 193°.

Preparation of N-(β-Acetanilinoethyl)-2-pyridone Hydrochloride (VI).—To 7.7 g. (0.036 mole) of IV in 600 ml. of benzene was added 3.14 g. (0.04 mole) of acetyl chloride. The addition was carried out at 5°. Crystallization of the precipitate from ethanol–ether provided 8.5 g. (80.6%) of VI, m.p. 118–124°.

Anal. Calcd. for $C_{15}H_{17}ClN_2O_2$: C, 61.53; H, 5.85; N, 9.57. Found: C, 61.46; H, 5.95; N, 9.66.

Titration of VI with standard potassium hydroxide gave a neutralization equivalent of 245 (calcd. for $C_{15}H_{17}ClN_2O_2$, 292.8). The pK_a value of the hydrochloride salt VI was determined as 2.65. Titration of VI with standard silver nitrate solution, using a potassium chromate indicator, provided a molecular weight of 267.

Preparation of N-(β-Acetanilinoethyl)-2-pyridone (VII).—A solution of 1.0 g. (0.0034 mole) of VI in 30 ml. of a 10:1 ether–alcohol mixture was treated with 0.34 g. (0.0034 mole) of triethylamine. Filtration of triethylamine hydrochloride followed by evaporation of the solution provided an oil which crystallized. Recrystallization from carbon tetrachloride provided 0.83 g. (95.4%) of VII, m.p. 100–104°.

When IV was allowed to react with 25 ml. of acetic anhydride followed by treatment with dilute sodium hydroxide, a brown oil was obtained. The oil was extracted with ether, the extract was evaporated, and the oil was allowed to crystallize. Recrystallization of the yellow solid from carbon tetrachloride provided VII, m.p. 104–105°, identical in all respects with the sample obtained from VI.

Hydrolysis of N-(β-Acetanilinoethyl)-2-pyridone (VII).—A 2.0-g. (0.007-mole) sample of VII was refluxed with 50 ml. of 25% sodium hydroxide solution for 26 hr. The brown oil was extracted with chloroform and the extracts were evaporated to provide 1.40 g. (93.3%) of IV as yellow needles, m.p. 109–111°. A mixture melting with a sample of IV prepared from II and III was not depressed. Acid hydrolysis of VI followed by neutralization provided a 73.3% yield of IV, m.p. 108–110°.

---

[7] Melting points and boiling points are uncorrected. Elemental analyses were by Micro-Tech Laboratories, Skokie, Ill.

[8] J. A. Berson and T. Cohen, *J. Am. Chem. Soc.*, **78**, 416 (1956); F. Ramirez and A. P. Paul, *J. Org. Chem.*, **19**, 183 (1954).

[9] E. H. Rodd, "Chemistry of Carbon Compounds," Vol. III, Elsevier Publishing Co., Amsterdam, 1954, p. 174.

[10] S. Okhi, *J. Pharm. Soc. Japan*, **70**, 101 (1950).

Exchange of Magnesium between the Ethyl Grignard Reagent and Magnesium Bromide[1a]

DWAINE O. COWAN, JOHN HSU,[1b] AND JOHN D. ROBERTS[1c]

Contribution No. 3148 from Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California

Received August 4, 1964

Much has been said but little settled about the precise nature of the Grignard reagent. The X-ray structure studies of Stucky and Rundle,[2] the vapor pressure studies of Vreugdenhil and Blomberg,[3] the work of Ashby and Becker,[4] and the far-infrared experiments of Salinger and Mosher[5] all indicate that the Grignard reagent can exist, at least in part, as a monomer (RMg-X) under a variety of experimental conditions. However, the nuclear magnetic resonance studies of Roos and Zeil,[6] the association studies of Slough and Ubbelohde[7] (concentrated solutions), plus the Grignard reaction studies of several groups (Bikales and Becker,[8] Mosher and co-workers,[9] House and Traficante,[10] Anteunis and D'Hollander,[11] Hamelin,[12] and Dessy and

---

[1] (a) Supported by the National Science Foundation; (b) National Science Foundation Undergraduate Fellow, summer, 1963; (c) to whom correspondence should be addressed at the Department of Chemistry, The Johns Hopkins University, Baltimore, Md. 21218.

[2] G. D. Stucky and R. E. Rundle, *J. Am. Chem. Soc.*, **85**, 1002 (1963).

[3] A. D. Vreugdenhil and C. Blomberg, *Rec. trav. chim.*, **82**, 453, 461 (1963).

[4] E. C. Ashby and W. E. Becker, *J. Am. Chem. Soc.*, **85**, 118 (1963).

[5] R. M. Salinger and H. S. Mosher, *ibid.*, **86**, 1782 (1964).

[6] H. Roos and W. Zeil, *Z. Elektrochem.*, **67**, 28 (1963).

[7] W. Slough and A. R. Ubbelohde, *J. Chem. Soc.*, 108 (1955).

[8] N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963).

[9] D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, **28**, 204 (1963); **27**, 1 (1962); J. Miller, G. Gregoriou, and H. S. Mosher, *J. Am. Chem. Soc.*, **83**, 3966 (1961).

[10] H. O. House and D. D. Traficante, *J. Org. Chem.*, **28**, 355 (1963).

[11] M. J. Anteunis and R. D'Hollander, *Tetrahedron Letters*, 1275 (1962).

[12] R. Hamelin, *Bull. soc. chim. France*, 915 (1961).

Salinger[13]) all indicate that the Grignard reagent in solution either consists in part of a dimeric species ($R_2Mg\cdot MgX_2$) or contains a mixture of dialkylmagnesium and magnesium halide ($R_2Mg + MgX_2$).

Dessy and co-workers[14] have studied the exchange of magnesium between Grignard species using isotopic labeling techniques. Magnesium bromide from magnesium-28 and bromine was mixed with diethylmagnesium prepared by the dioxane-precipitation method. Precipitation of the magnesium bromide from the solution with dioxane followed by isotopic analysis showed only 6 to 8% exchange of the labeled magnesium. From this, it was concluded that "the ethyl Grignard reagent is better represented by a complex $Et_2Mg\cdot MgBr_2$ than by EtMgBr" and that equilibrium 1 in ether is "at

$$2\mathrm{EtMgBr} \rightleftharpoons \mathrm{Et_2Mg} + \mathrm{MgBr_2} \text{ or } (\mathrm{Et_2Mg\cdot MgBr_2}) \qquad (1)$$

most a very unimportant side reaction." In a later paper[15] it was reported that substitution of the stable isotope magnesium-25 for magnesium-28 gave a statistical distribution of magnesium but that this exchange could be caused by an impurity in the magnesium-25.

We have carried out a somewhat different type of exchange experiment with high-purity magnesium-25 and observed statistical exchange. Magnesium-25 bromide, prepared from magnesium-25 and ethylene dibromide, was added directly to a Grignard reagent prepared from Dow Grignard magnesium and ethyl bromide in ethyl ether. This procedure precludes questions as to whether a mixture of diethylmagnesium and magnesium bromide is equivalent to a Grignard reagent and furthermore avoids having impurities such as dioxane which might arise in the preparation of the diethylmagnesium. After 1.5 hr., the magnesium bromide was precipitated from the solution with dioxane washed with ether and converted to magnesium oxide; the proportions of magnesium-24, -25, and -26 were determined by mass spectrographic analysis.[16] The results indicate that statistical equilibrium is achieved among the various forms of magnesium present. Therefore, if the Grignard reagent is to be represented as $Et_2Mg\cdot MgBr_2$, exchange of magnesium-25 occurs not only with the complexed magnesium bromide, but also with the dialkylmagnesium. The impurities in Dow Grignard grade magnesium and the impurities in the magnesium-25 used are listed in Table I. It must be concluded that under these conditions exchange does in fact take place, either by way of the equilibrium 1 or some equivalent process.

After the completion of the above experiments, Dessy and co-workers[17] published the results of a number of exchange studies that are in general agreement with ours save for those carried out with one maverick variety of magnesium, Dow atomized shot, which was reported to give no exchange. The unusual character of this sample of the metal in the exchange is not understood; however, as will be reported in more detail elsewhere, 3,3-dimethylbutylmagnesium chloride prepared from Dow atomized shot has been shown by Dr. George M. Whitesides to give the triplet n.m.r. resonances of the α-protons which characterize very rapid loss of configurational stability.[18] This lack of configurational stability could well be associated with exchange of alkyl groups by processes such as eq. 1, but this has not been established.

TABLE I

IMPURITIES IN MAGNESIUM

Element	Dow Grignard grade,[a] %	Mg^{25},[b] %
Al	0.005	0.02
Ca	. . .	0.01
Cu	<0.02	0.01
Mn	<0.15	c
Ni	<0.001	c
Fe	0.03	0.02
Pb	<0.01	c
Si	0.002	0.05
Sn	<0.01	c

[a] F. J. Krenzke, J. W. Hays, and D. L. Spell [*J. Metals*, **10**, 28 (1958)] give maximum and typical analysis for Dow magnesium. [b] Analysis performed by the Analytical Chemistry Division of Oak Ridge National Laboratory. [c] Not detected.

Experimental

Ethyl Grignard Reagent and Magnesium-25 Bromide.—A 1 *N* solution of the Grignard reagent from ethyl bromide was prepared in the usual manner using Dow Grignard magnesium. The reaction of ethyl bromide and magnesium was initiated by warming (no catalyst was used) and Grignard dried ether was used for the reaction. The Grignard reagent was analyzed for basic magnesium by acid titration to a phenolphthalein end point.

Magnesium-25 obtained from the Stable Isotopes Department of the Oak Ridge National Laboratory, 100 mg., was placed in a dry 10-ml. conical flask fitted with a small condenser. An inlet tube on the upper portion of the flask, closed by a rubber serum-bottle cap, allowed reagents to be added and later samples to be withdrawn. After the flask had been dried by concurrently flushing with nitrogen and heating with a cool Bunsen flame, 4 ml. of Grignard dried ether and 345 μl. of ethylene dibromide were added using hypodermic syringes. The reaction was initiated only after warming and crushing the magnesium chips with a stirring rod. The reaction mixture, protected from the atmosphere by a Gilman trap, was warmed (30°) for 2 hr. and allowed to stand overnight at room temperature.[19] The lower phase of the two-phase solution was used in the exchange experiment.

Equilibration of Magnesium-25 Bromide and Ethyl Grignard Reagent.—To a dried, nitrogen-flushed and serum-bottle-capped, 3-ml. centrifuge tube was added 1 ml. of the standardized 1 *N* Grignard reagent prepared from ethyl bromide (1×10^{-3} moles of EtMgBr) and 115 μl. (3.0×10^{-4} moles of $MgBr_2$) of the lower phase of the labeled magnesium bromide solution. Any increase in pressure in the centrifuge tube at this step or later was vented with a hypodermic needle attached to a Gilman trap. The tube was shaken to ensure homogeneity and allowed to stand for 1.5 hr. Magnesium bromide was precipitated by the slow addition of 165 μl. of purified anhydrous dioxane. During this time, the tube was vigorously shaken and intermittently cooled. The magnesium bromide didioxanate was separated from the resulting slurry by centrifugation and the diethylmagnesium solution was withdrawn with a hypodermic syringe. To wash the precipitate, Grignard dried ether (0.5 ml.) was added to the centrifuge tube containing the magnesium bromide precipitate and the mixture was suspended by shaking. The precipitate was separated again by centrifugation and the ether withdrawn. This procedure was repeated twice. Mass spectrographic analysis[16] of the precipitated magnesium indicated the following isotopic abundance:

---

(13) R. E. Dessy and R. M. Salinger, *J. Am. Chem. Soc.*, **83**, 3530 (1961).

(14) R. E. Dessy, G. S. Handler, J. H. Wotiz, and C. A. Hollingsworth, *ibid.*, **79**, 3476 (1957).

(15) R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1958).

(16) Mass spectrographic analyses were performed by the Mass Spectrometer Laboratory, Oak Ridge National Laboratory.

(17) R. E. Dessy, S. E. I. Green, and R. M. Salinger, *Tetrahedron Letters*, **No. 21**, 1369 (1964).

(18) G. M. Whitesides and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 2167 (1963).

(19) Part of the magnesium did not react and a sample of this was analyzed by the Analytical Chemistry Division of the Oak Ridge National Laboratory. The residue was primarily magnesium with larger amounts of impurities than listed in Table I. Carbon that may have been introduced in the reduction of magnesium oxide to magnesium would not have been detected by the analytical procedure used.

Mg^{24}, 59.9%; Mg^{25}, 31.6%; and Mg^{26}, 8.4%; while the isotopic abundance of the magnesium-25 used was Mg^{24}, 0.43%; Mg^{25}, 99.49%; Mg^{26}, 0.09%. A simple calculation using this data and the natural isotope abundance for the Grignard magnesium indicates a statistical distribution of magnesium-24, -25, and -26.

Reaction of Benzoyl Chloride with Triphenyltin Hydride

EUGENE J. KUPCHIK AND ROBERT J. KIESEL

Department of Chemistry, St. John's University, Jamaica 32, New York

Received June 19, 1964

A recent report by Kuivila[1] on the reaction of benzoyl chloride with tri-*n*-butyltin hydride has prompted us to report our results on the reaction of benzoyl chloride with triphenyltin hydride.

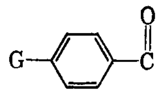
Kuivila has reported that reduction of benzoyl chloride with tri-*n*-butyltin hydride in ether gives benzaldehyde (54%) as the major reduction product; in the absence of solvent, benzyl benzoate (58%) predominates. He also has presented evidence which suggests a free-radical mechanism for this reaction. Van der Kerk, *et al.*,[2] have reported that benzaldehyde, identified as the 2,4-dinitrophenylhydrazone, and triphenyltin chloride are formed when benzoyl chloride is heated with triphenyltin hydride; no yields or detailed experimental conditions were given.

We have found that, when triphenyltin hydride and benzoyl chloride are mixed at room temperature and allowed to react at the ambient temperature, the major products formed are triphenyltin chloride and benzyl benzoate; a minor product is benzene. The results of several runs carried out under a variety of conditions are summarized in Table I. In no case could benzaldehyde be detected, either as the 2,4-dinitrophenylhydrazone, or by using gas–liquid chromatography. In a control experiment it was found that as little as 2% of benzaldehyde could be recovered as the 2,4-dinitrophenylhydrazone in 90% yield. Control experiments were always run whenever gas–liquid chromatography was employed.

The minor product of the reaction, benzene, could have originated from the benzoyl chloride or the triphenyltin hydride or from both of these compounds. Benzene has been observed as a product in several other triphenyltin hydride reactions in which it could have arisen only from the hydride.[3-5] It appears likely that it originated from the triphenyltin hydride in this case also since it was also a minor product (10% yield) of the reaction between triphenyltin hydride and *p*-methylbenzoyl chloride; no toluene was formed in this reaction, as revealed by gas–liquid chromatography. The major products were triphenyltin chloride (80.4%) and *p*-tolyl *p*-toluate (73.6%); again, no aldehyde was present as evidenced by gas–liquid chromatography and the absence of a 2,4-dinitrophenylhydrazone.

In order to determine whether the reaction of benzoyl chloride with triphenyltin hydride proceeds by an ionic or a radical mechanism it was carried out in the presence of three well-known radical inhibitors: hydroquinone,[6] *trans*-stilbene,[7] and galvinoxyl[8]; it was also carried out in the presence of azobisisobutyronitrile, a well-known radical initiator.[9] It was found that the reaction was retarded by each of the inhibitors employed and accelerated by the azobisisobutyronitrile. This result is consistent with a radical mechanism. The results are summarized in Table II.

There is an indication that electron-releasing substituents facilitate the reaction whereas electron-withdrawing substituents hinder the reaction. The results are summarized in Table III. Both electron-releasing substituents and electron-withdrawing substituents would be expected to stabilize a possible radical intermediate such as I. Our results indicate that other factors besides the stabilization of I are important in determining the rate of the reaction.



I

It should be noted that the *p*-nitrobenzoyl chloride was unreactive even in the presence of azobisisobutyronitrile. In this case the *p*-nitrobenzoyl chloride may act as its own inhibitor since nitro compounds are known to inhibit radical reactions.[10]

Experimental

Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected. Each triphenyltin hydride reaction was carried out in an atmosphere of prepurified nitrogen (Matheson). The triphenyltin chloride obtained in each reaction was identified by mixture melting point determination and infrared spectral comparison with a known sample. The acid chlorides used were all commercially available and were freshly distilled before use with the exception of *p*-nitrobenzoyl chloride which was recrystallized from *n*-hexane.

Gas–liquid chromatography data were obtained on a Perkin-Elmer vapor fractometer Model 154B. The reaction mixtures were dissolved in diethyl ether, and a 10-μl. portion of the solution was used. The per cents of benzaldehyde and benzene were determined using a diisodecyl phthalate column at 100° and a flow rate of 55 cc. of He/min. The per cents were estimated by comparison with standard chromatograms.

Reaction of Benzoyl Chloride with Triphenyltin Hydride. A. In the Absence of Inhibitors and Accelerators.—Triphenyltin hydride (82.0 g., 0.205 mole) and benzoyl chloride (28.9 g., 0.205 mole) were mixed at room temperature and allowed to react at the ambient temperature for 24 hr., after which time the mixture had become a thick white paste. The reaction mixture was connected to a Dry Ice–acetone trap and heated to 100° (12 mm.). In the trap was found 0.80 g. of a liquid whose infrared spectrum was superimposable on that of an authentic sample of benzene.

---

(1) H. G. Kuivila in "Advances in Organometallic Chemistry," Vol. I, F. G. A. Stone and R. West, Ed., Academic Press, New York, N. Y., 1964, p. 81.

(2) G. J. M. van der Kerk, J. G. Noltes, and J. G. A. Luijten, *J. Appl. Chem.* (London), **7**, 356 (1957).

(3) A. Stern and E. I. Becker, *J. Org. Chem.*, **27**, 4052 (1962).

(4) S. Weber and E. I. Becker, *ibid.*, **27**, 1258 (1962).

(5) F. J. Kupchik and R. J. Kiesel, *ibid.*, **29**, 764 (1964).

(6) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 431.

(7) C. G. Swain, W. H. Stockmayer, and J. T. Clarke, *J. Am. Chem. Soc.*, **72**, 5426 (1950).

(8) F. D. Greene, W. Adam, and J. E. Cantrill, *ibid.*, **83**, 3461 (1961).

(9) See ref. 6, p. 70.

(10) See ref. 6, p. 168.