red. IIa showed $\lambda_{C=O}^{CHCl_3}$ 5.95 μ; n.m.r. 140 (s, $-CH_3$), 271 (s, NCH_2S), 144 (m, NCH_2), and 89 (m, CCH_2) c.p.s. in CCl_4; IIb showed $\lambda_{C=O}^{CHCl_3}$ 6.00 μ; n.m.r. 479 and 486 (d, *ortho* =CH—), 449 (m, *meta* and *para* =CH—), 287 (s, NCH_2S), 150 (m, NCH_2), and 87 (m, CCH_2) c.p.s. in CCl_4.

Rearrangement of 1-Piperidinemethanethiol Acetate (IIa) to 1-Acetylpiperidine (IIIa).—A solution of 7.6 g. (0.044 mole) of 1-piperidinemethanethiol acetate (IIa) in 25 ml. of benzene was prepared. The solution was heated for 12 hr. The residue on distillation afforded 2.18 g. (60%) of 1-acetylpiperidine, b.p. 56–60° at 1.0 mm. (lit.[4] b.p. 226–227° at 760 mm.). The infrared and n.m.r. spectra of this substance were identical with those of an authentic sample: $\lambda_{C=O}^{CHCl_3}$ 6.14 μ; n.m.r. 117 (s, $-CH_3$), 205 (m, NCH_2), and 96 (m, CCH_2) c.p.s. in CCl_4.

Rearrangement of 1-Piperidinemethanethiol Benzoate (IIb) to 1-Benzoylpiperidine (IIIb).—The same procedure was used in the rearrangement of IIa. A solution of 8.2 g. (0.034 mole) of 1-piperidinemethanethiol benzoate (IIb) afforded 3.30 g. (50%) of 1-benzoylpiperidine, b.p. 118–120° at 1.0 mm., m.p. 46–47° (lit.[4] b.p. 320–321° at 760 mm., m.p. 48°). The mixture melting point, infrared, and n.m.r. spectra of this substance were identical with those of an authentic sample: $\lambda_{C=O}^{CHCl_3}$ 6.18 μ; n.m.r. 439 (s, all =CH—), 206 (m, NCH_2), and 94 (m, CCH_2) c.p.s. in CCl_4.

Polymeric Thioformaldehyde.—The undistillable residue obtained in the rearrangement of IIa and IIb was recrystallized from $CHCl_3$. The yield was 0.98 g. (48%) of a mixture of polymeric forms of thioformaldehyde, m.p. 136–145°, in the rearrangement of IIa and 0.71 g. (45%) in the rearrangement of IIb [lit.[5] m.p. 175–176° for $(CH_2S)_x$, m.p. 216° for $(CH_2S)_3$]. No attempt was made to isolate trithiane from the mixture or to characterize the other thioformaldehyde polymers.

Acknowledgment.—The authors gratefully acknowledge the support of this project by the National Institutes of Health Grants 1-F1-GM 14, 467-01A2, and RG-9254.

(4) "Dictionary of Organic Compounds," I. M. Heilbron, *et. al.*, Ed., Oxford University Press, New York, N. Y., 1953.

(5) A. Wohl, *Ber.*, **19**, 2344 (1886).

The Chemistry of Carbanions. VII. The Stereochemistry of Addition of Various Methylmagnesium Reagents[1]

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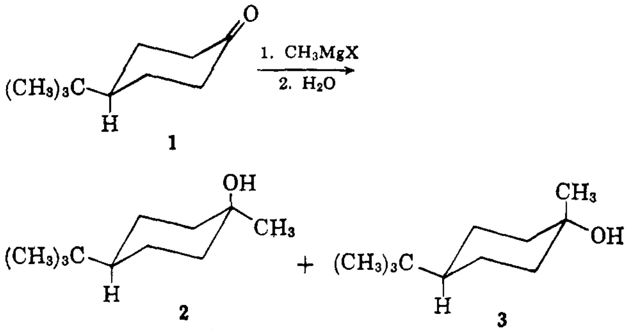
Earlier studies[2,3] of additions of organomagnesium compounds to ketones had demonstrated that dialkylmagnesium compounds are more reactive than alkylmagnesium halides (Grignard reagents). Either organometallic reactant, when in excess, produces the same proportion of addition product to by-products resulting from enolization or reduction. However, the organometallic reagent, corresponding stoichiometrically to an alkylmagnesium alkoxide, obtained from reaction of 1 mole of a dialkylmagnesium with either 1 mole of a ketone or 1 mole of a tertiary alcohol produced much greater proportions of by-products from enolization and reduction on reaction with simple ketones.[3] This latter result was observed only when the alkylmagnesium alkoxide reagent was free from magnesium halide. One interpretation of these results is that all of the reactions in the presence of magnesium halide as well as reactions employing an excess of a dialkylmagnesium each involve the same organomagnesium species, perhaps a dialkylmagnesium, as the actual reacting species, whereas reactions with halide-free alkylmagnesium alkoxides involve a different reacting species which may be either an alkylmagnesium alkoxide or some more complex structure. To examine this hypothesis further we have examined the n.m.r. spectra of various organomagnesium reagents, a study to be reported elsewhere, and have studied the stereochemical course of additions of various methylmagnesium derivatives to a ketone to learn if differences could be detected.

This latter study, reported here, utilized the reaction of various methylmagnesium derivatives with 4-*t*-butylcyclohexanone (**1**) to form the *cis*- (**2**) and *trans*-carbinols (**3**).[4] In this reaction we wished to take advantage of the seemingly valid generalization[5] that use of a more hindered cyclohexanone derivative or use of a more hindered organometallic reagent can be expected to increase the proportion of the cyclohexanol isomer with an axial hydroxyl function and an equatorial alkyl group (corresponding to **2**). From the proportions of isomers **2** and **3** formed we might hope to learn whether the reacting species derived from various methylmagnesium reagents were different. The results of this study are summarized in Table I which lists the average values obtained from two or more determinations. All reaction mixtures obtained from organomagnesium reagents in the presence of magnesium bromide or with excess dimethylmagnesium yielded predominantly a mixture of alcohols **2** and **3** with little enolization (as measured by the amount of ketone **1** recovered). The products of these reactions contained 55–65% of the axial alcohol **2**. From reaction mixtures containing the halide-free methylmagnesium salt of 3-methyl-3-pentanol, a large amount



1

2 (*cis*, m.p. 70-71°)

3 (*trans*, m.p. 96.5-97°)

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(1) This research has been supported by research grants from the National Institutes of Health (R. G. 8761) and the National Science Foundation (G-25214).

(2) (a) J. G. Aston and S. A. Bernhard, *Nature*, **165**, 485 (1950); (b) D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, **27**, 1 (1962); **28**, 204 (1963); (c) M. Anteunis, *ibid.*, **26**, 4214 (1961); **27**, 596 (1962); M. Anteunis and R. D'Hollander, *Tetrahedron Letters*, **No. 26**, 1275 (1962); (d) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963); (e) A. Kirrmann, M. Vallino, and J. F. Fauvarque, *Bull. soc. chim. France*, 1408 (1963).

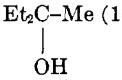
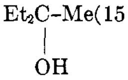
(3) (a) H. O. House, D. D. Traficante, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963); (b) H. O. House and D. D. Traficante, *ibid.*, **28**, 355 (1963); (c) H. O. House and H. W. Thompson, *ibid.*, **28**, 360 (1963).

(4) (a) B. Cross and G. H. Whitham, *J. Chem. Soc.*, 3892 (1960); (b) C. H. DePuy and R. W. King, *J. Am. Chem. Soc.*, **83**, 2743 (1961); (c) W. J. Houlihan, *J. Org. Chem.*, **27**, 3860 (1962); (d) H. Favre and D. Gravel, *Can. J. Chem.*, **39**, 1548 (1961).

(5) (a) G. Just and R. Nagarajan, *Experientia*, **18**, 402 (1962); (b) G. F. Hennion and F. X. O'Shea [*J. Am. Chem. Soc.*, **80**, 614 (1958)] found that addition of ethylmagnesium bromide to **1** gave product containing 73% of the product with an axial hydroxyl function (corresponding to **2**), whereas use of methylmagnesium bromide produced a mixture containing 55–60% of the corresponding isomer **2** (ref. 4 and this study).

TABLE I

REACTION OF 4-*t*-BUTYLCYCLOHEXANONE WITH METHYLMAGNESIUM DERIVATIVES

Ketone, mmoles	Magnesium derivative (mmoles)	Additive (mmoles)	Volume of soln., ml.	Yield of alcohol, %	Recovery of ketone, %	Composition of alcohol mixture[a] % *cis*	% *trans*
9.2	MeMgBr (37)	...	37	94–96	...	60	40
7.8	Me_2Mg (15.5)	...	31	83	8–9	65	35
7.8	Me_2Mg (15.5)	$MgBr_2$ (15.6)	31	92–93	...	60	40
4.2	Me_2Mg (8.5)	$MgBr_2$ (10.8)	28.6	95–97	...	61	39
8.3	MeMgBr (33)	Et–CO–Et (16.5)	33	89–94	...	55	45
8.3	MeMgBr (33)	 $\underset{OH}{Et_2C}{-}Me$ (16.5)	33	88–93	...	57	43
7.8	Me_2Mg (15.5)	Et–CO–Et (15.5) + $MgBr_2$ (15.6)	31	87–91	2–4	60	40
7.8	Me_2Mg (15.5)	 $\underset{OH}{Et_2C}{-}Me$(15.5)	31	28–30	48–51[b]	73	27
7.8	Me_2Mg (15.5)	Et–CO–Et (15.5)	31	23–30	46–52[b]	75	25

[a] Average values from two or more runs are listed. The individual values obtained did not differ from these average values by more than ±2%. [b] See the Experimental section for a description of other products present.

of enolization was observed as measured by the amount of recovered ketone **1** and by the formation of higher molecular weight products from aldol condensation (see Experimental). The alcohol product contained 73–75% of the axial alcohol **2**. Although the stereochemical differences observed in these reactions are not large, the results are compatible with our early suggestion[3] that the reacting species in halide-free solutions of alkylmagnesium alkoxides is not the same as the reacting species derived from Grignard reagents or dialkylmagnesium compounds. The data would suggest that the reacting species obtained from the alkylmagnesium alkoxide has the greater steric bulk.

Experimental[6]

Preparation of Reagents.—Ethereal solutions of methylmagnesium bromide, dimethylmagnesium (from dimethylmercury), and magnesium bromide (from ethylene dibromide) were prepared and standardized as previously described.[3] Reaction of 14.02 g. (0.163 mole) of 3-pentanone with 250 ml. of an ethereal solution containing 0.330 mole of methylmagnesium bromide yielded, after the usual isolation procedure and fractional distillation, 10.06 g. (60%) of pure[7] 3-methyl-3-pentanol, b.p. 120–121°, $n^{25}D$ 1.4158 [lit.[8] b.p. 120–123°, $n^{25}D$ 1.4153], infrared[9] absorption 3610 and 3450 cm.$^{-1}$ (unassocd. and assocd. O–H). Ethereal solutions of methylmagnesium 3-methyl-3-pentoxide (or its equivalent) were obtained by adding 1 molar equiv. of either 3-pentanone or 3-methyl-3-pentanol to an ethereal solution containing either 1 molar equiv. of dimethylmagnesium or 2 molar equiv. of methylmagnesium bromide. The resulting solutions were stirred under nitrogen for 1 hr. prior to use. Pure[7] 4-*t*-butylcyclohexanone, b.p. 61–62° (0.1 mm.), m.p. 46–48° (lit.[10] m.p. 47.5–48.5°), infrared[9] absorption 1730 cm.$^{-1}$ (C=O), n.m.r.[9] absorption δ 0.92 (singlet, 9H, CH_3) and 1.3–2.5 (broad multiplet, 9H), was obtained by oxidation of the commercially available mixture of 4-*t*-butylcyclohexanols with chromic acid in acetic acid. The reaction of 4-*t*-butylcyclohexanone with an ethereal solution of methylmagnesium iodide at room temperature for 2 hr., followed by the usual isolation procedure, yielded, after sublimation (25° at 0.1 mm.), 64% of a mixture[11] of the stereoisomeric 1-methyl-4-*t*-butylcyclohexanols, m.p. 55–58°. Chromatography of 2.2 g. of this mixture on 150 g. of Merck acid-washed alumina separated 1.04 g. of the *cis* alcohol (first eluted with benzene–ether mixtures), m.p. 68–70°, and 0.969 g. of the *trans* alcohol (second eluted with benzene–ether mixtures), m.p. 95–96°. Recrystallization of each of these fractions from aqueous methanol afforded the *cis* isomer as white needles, m.p. 70–71° (lit.[4c] m.p. 71°), and the *trans* isomer as white prisms, m.p. 96.5–97° (lit.[4c,d] m.p. 97–98°).

The pure[7] *cis* isomer (eluted first on gas chromatography) has infrared absorption[9] at 3610 and 3480 cm.$^{-1}$ (O–H) with n.m.r. singlets[12] at δ 0.88 (9H) and at 1.21 (3H) as well as broad absorption in the region 1.2–1.9 (9H). The pure[7] *trans* isomer (eluted second on gas chromatography) has infrared peaks[9] at 3605 and 3350–3450 cm.$^{-1}$ (OH) with n.m.r. singlets[1] at δ 0.88 (9H) and at 1.23 (3H) and broad absorption in the region 1.0–2.0 (9H).

Quantitative Reactions of Methylmagnesium Derivatives with 4-*t*-Butylcyclohexanone.—All reactions were run under a nitrogen atmosphere. For the gas chromatographic analyses,[13] calibration curves were prepared from mixtures of known composition containing the various reactants and products. An ethereal solution containing ketone was added to an ethereal solution of the methylmagnesium derivative containing any additives specified in Table I. During the addition the reaction mixture was cooled by use of an ice bath. After the addition was complete, the reaction mixture was stirred for 1 hr. and then a weighed amount of durene was added as an internal standard and the mixture was hydrolyzed with saturated aqueous ammonium chloride. The ether layer and ether washings of the aqueous phase were combined, dried, concentrated under a Vigreux column, and analyzed. The results are summarized in Table I in which molar quantities from a representative run are cited with the range of yields obtained and the average composition of the product mixture. In none of the experiments cited did the composition of an individual run differ from the average value by more than ±2%.

The material balances obtained were of the order of 90% for all of the reactions studied except the last two listed in Table I. In these cases where enolization (leading to recovery of the starting ketone after hydrolysis) was the predominant reaction, approximately 80% of the reactants were accounted for as recovered ketone or alcohol products. The reaction mixtures from a number of these runs were combined and distilled to separate a low-boiling fraction, b.p. 38–39° (16 mm.), composed largely of 3-methyl-3-pentanol as judged from its infrared spectrum. The

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(6) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer, Model 237, infrared recording spectrophotometer fitted with a grating. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(7) A gas chromatography column packed with 20 M Carbowax suspended on ground firebrick was employed for this analysis.

(8) W. G. Young and I. D. Webb, *J. Am. Chem. Soc.*, **73**, 780 (1951).

(9) Determined in carbon tetrachloride solution.

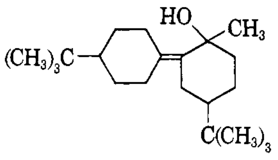
(10) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

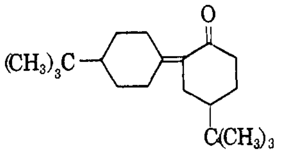
(11) A thin layer chromatographic plate coated with silica gel was employed for this analysis. The eluent was 2:1 (by volume) petroleum ether–ethyl ether.

(12) Determined as a solution in deuteriochloroform.

(13) A column packed with General Electric silicone gum, No. XE-60, suspended on Chromosorb W was employed.

residue from this distillation was sublimed (25° at 0.1 mm.) for 48 hr. to separate the bulk of the volatile products, 4-*t*-butylcyclohexanone and the stereoisomeric 4-*t*-butyl-1-methylcyclohexanols. The residue from this sublimation was recrystallized from cyclohexane to separate a white crystalline solid melting over the range 139-190° which exhibited a single broad peak when examined by gas chromatography.[14] Since we were unsuccessful in obtaining a single pure substance from the high molecular weight material, the spectra of the mixture were examined. The mixture has infrared absorption[15] at 3580 and 3450 cm.$^{-1}$ (unassocd. and assocd. OH) with no absorption in the 6-μ region attributable to a carbonyl function. The n.m.r. spectrum[12] has a singlet at δ 0.82 (CH_3–C<) with broad, partially resolved absorption in the region 1.0–1.8 but no evidence of absorption at lower field indicative of vinyl protons. The mass spectrum[16] was particularly informative, exhibiting the highest peak at m/e = 306 (M^+) with high mass fragment peaks at 291 (M − 15), 288 (M − 18), 273 (M − 15 − 18, abundant), 249 (M − 57, abundant), and 231 (M − 57 − 18, abundant), and an intense peak at m/e = 57. These data are most easily accommodated by one or more of the stereoisomers of the structure **4** which would be expected to arise by an initial aldol condensation of 4-*t*-butylcyclohexanone with itself to form the ketone **5** followed by reaction with the methylmagnesium species present in solution.


4


5

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[14] A column packed with silicone gum, No. SE-30, suspended on Chromosorb W was employed.

[15] Determined as a solution in chloroform.

[16] Determined with a CEC, Model 21-103, mass spectrometer.

Some New Condensation Products in the Reaction of Diethylmagnesium with Benzonitrile

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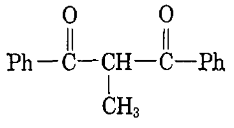
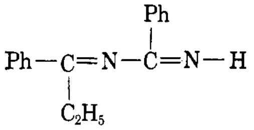
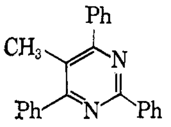
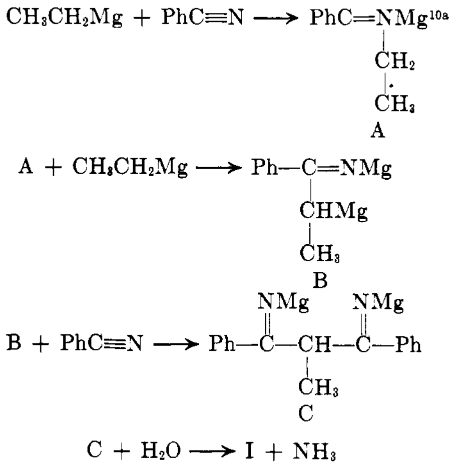
We wish to report three new condensation products from the reaction of diethylmagnesium with benzonitrile. While condensation products are well known in the reactions of alkylmagnesium compounds with nitriles, these have heretofore been observed only when either the nitrile[2] or the Grignard reagent[3] is unsaturated or when the nitrile contains active α-hydrogen atoms.[4–8] Trimerization of the nitrile to form an *s*-triazine has also been observed.[9]

From the reaction between diethylmagnesium and benzonitrile in tetrahydrofuran, when the ratio of available ethyl groups to benzonitrile was 1 or smaller, 1,3-diphenyl-2-methyl-1,3-propanedione (I) and 5-methyl-2,4,6-triphenylpyrimidine (III) were isolated. From the same reactants in ethyl ether a substance which appears to be N-(α-ethylbenzal)benzamidine (II) as well as the pyrimidine (III) were isolated. I was assumed to have formed by hydrolysis of the corresponding bisketimine salt initially formed in the reaction mixture. The origin of the bisketimine salt is reasonably represented as an aldol-type of condensation in the "nitrogen system." To our knowledge this type of reaction has been observed only once previously. Ectors[10b] has isolated 3,4,5-triphenyl-Δ^2-pyrazoline as a product in the reaction of benzylmagnesium chloride with benzonitrile. It is likely that this product is formed by attack of a salt similar to B upon another molecule of benzonitrile, followed by cyclization.


I


II


III



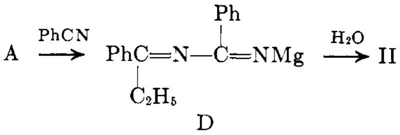
$$\mathrm{CH_3CH_2Mg + PhC{\equiv}N \longrightarrow \underset{\substack{|\\ CH_2\\ |\\ CH_3\\ A}}{PhC{=}NMg}^{10a}}$$

$$\mathrm{A + CH_3CH_2Mg \longrightarrow Ph{-}\underset{\substack{|\\ CHMg\\ |\\ CH_3\\ B}}{C}{=}NMg}$$

$$\mathrm{B + PhC{\equiv}N \longrightarrow Ph{-}\overset{\substack{NMg\\ \|}}{C}{-}\underset{\substack{|\\ CH_3\\ C}}{CH}{-}\overset{\substack{NMg\\ \|}}{C}{-}Ph}$$

$$\mathrm{C + H_2O \longrightarrow I + NH_3}$$

Formation of the benzamidine, II, is readily understood as arising from the addition of A to a second molecule of benzonitrile to give a new salt D.[11] Hydrolysis of D gives II.



$$\mathrm{A \xrightarrow{PhCN} Ph\underset{\substack{|\\ C_2H_5}}{C}{=}N{-}\overset{\substack{Ph\\ |}}{C}{=}NMg \xrightarrow{H_2O} II}$$
D

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[1] (a) This material was abstracted from part of the doctoral dissertations of N. M. B. (1961) and A. A. S. (1965) presented to the Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements of their Ph.D. degrees. (b) To whom inquiries should be sent.

[2] H. R. Henze and L. R. Swett, *J. Am. Chem. Soc.*, **73**, 4918 (1951).

[3] H. R. Henze, G. L. Sutherland, and G. D. Edwards, *ibid.*, **73**, 4915 (1951).

[4] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall Co., Inc., New York, N. Y., 1954, pp. 774-776, 782-783.

[5] C. R. Hauser and W. J. Humphlett, *J. Org. Chem.*, **15**, 359 (1950).

[6] J. Decombe, *Compt. rend.*, **234**, 2542 (1952).

[7] M. Pretot and J. Decombe, *ibid.*, **244**, 1512 (1957).

[8] F. F. Blicke and E. P. Tsao, *J. Am. Chem. Soc.*, **75**, 5587 (1953).

[9] J. D. Citron and E. I. Becker, *Can. J. Chem.*, **41**, 1260 (1963).

[10] (a) The second valence of magnesium is unspecified. (b) E. Ectors, *Bull. soc. chim. Belges.*, **33**, 146 (1924).

[11] J. J. Ritter and R. D. Anderson [*J. Org. Chem.*, **24**, 208 (1959)] assumed a similar type of condensation in the polymerization of benzonitrile with sodium.