g. (0.08 mole) of *p*-chlorobromobenzene in 310 ml. of ether. The product was recovered as above to yield 9.9 g. (71%) of product, m.p. 47°. A mixed melting point with the product from (A) showed no depression.

Direct Chlorination of Dimethylbis-(*p*-chlorophenyl)-silane.—Seven grams (0.0249 mole) of dimethylbis-(*p*-chlorophenyl)-silane was treated with chlorine under the same conditions as those used for methyltris-(*p*-chlorophenyl)-silane. During the chlorination, some crystals which sublimed onto the condenser were identified as *p*-dichlorobenzene by mixed melting point. After the reaction mixture plus the trap contents had gained 2.65 g. in weight (equivalent to 0.0736 g. atom of chlorine) the mixture was flushed with nitrogen. No crystals formed on cooling or on extraction with methanol. On distillation at 50 mm. a white solid sublimed on to the condenser. This solid melted at 53.4° and was identified as *p*-dichlorobenzene by a mixed melting point with an authentic specimen. The residue became dark on continued heating and no other product was isolated.

Another 5 g. (0.0178 mole) of dimethylbis-(*p*-chlorophenyl)-silane was dissolved in 20 ml. of carbon tetrachloride and treated with a rapid stream of chlorine for 2 hours at gentle reflux temperature with ultraviolet irradiation. The carbon tetrachloride was removed on a steam-cone leaving a viscous liquid which would not crystallize from methanol solution. An attempt to distil the liquid at 1 mm. resulted in some decomposition taking place above 200°. Two grams of clear distillate was obtained under high vacuum, b.p. 165–170° at 0.00001 mm.; n^{20}_{D} 1.6062, d^{20}_{4} 1.349; MR_{D} calcd.[18] for methyl-(dichloromethyl)-bis-(*p*-chlorophenyl)-silane, 89.14; obsd., 89.54.

Anal. Calcd. for $C_{14}H_{12}Cl_4Si$: Cl, 40.4. Found: Cl, 39.7. (The calculated chlorine analysis for methyl-(trichloromethyl)-bis-(*p*-chlorophenyl)-silane is 46.1%.)

A similar chlorination carried out at 50° without solvent, also yielded only the dichlorinated derivative.

Chlorination of Dimethylbis-(*p*-chlorophenyl)-silane with Sulfuryl Chloride.—To 10 g. (0.0356 mole) of dimethylbis-(*p*-chlorophenyl)-silane dissolved in 20 ml. of carbon tetrachloride was added 6.75 g. (0.05 mole) of sulfuryl chloride and 0.1 g. of benzoyl peroxide. The solution was refluxed for 5 hours in a dry atmosphere. The product was fractionated through a wire spiral column to yield 8 g. of light straw-colored liquid, b.p. 160–170° at 0.2 mm.; n^{20}_{D} 1.5978.

Anal. Calcd. for $C_{14}H_{13}Cl_3Si$: Cl, 33.5. Calcd. for $C_{14}H_{12}Cl_4Si$: Cl, 40.4. Found: Cl, 35.6.

The analysis indicates that this product is a mixture of methyl-(mono- and dichloromethyl)-bis-(*p*-chlorophenyl)-silane.

Another 10 g. (0.0356 mole) of dimethylbis-(*p*-chlorophenyl)-silane in 20 ml. of carbon tetrachloride was refluxed with 20.25 g. (0.15 mole) of sulfuryl chloride and 0.2 g. of benzoyl peroxide for 16 hours. Fractionation of the product gave 7.0 g. of liquid, b.p. 170° at 0.1 mm.; n^{20}_{D} 1.6068. This refractive index corresponds closely to that of the methyl-(dichloromethyl)-bis-(*p*-chlorophenyl)-silane previously identified.

An attempt was made to prepare methyl-(trichloromethyl)-bis-(*p*-chlorophenyl)-silane by another method. Methyl-(trichloromethyl)-dichlorosilane, was prepared in 58% yield by the method of Krieble and Elliott[4] using an excess of chlorine. Treatment of this latter material with *p*-chlorophenyllithium at room temperature gave none of the desired product. Again *p*-dichlorobenzene was formed on attempted distillation of the product.

(Trichloromethyl)-triphenylsilane.—Forty grams (0.1457 mole) of methyltriphenylsilane[3] was treated with chlorine at 150°, with ultraviolet irradiation, in the apparatus used for the chlorination of methyltris-(*p*-chlorophenyl)-silane. The chlorination was continued until the weight increase was 15.5 g., equivalent to 0.437 g. atom of chlorine. On cooling, the mixture solidified. This solid was extracted three times with hot methanol and then crystallized from a benzene–petroleum ether (b.p. 77–122°) mixture to yield 21.2 g. (38.6%) of a white solid, melting at 192–194°. Two further crystallizations from petroleum ether (b.p. 77–122°) gave white needles melting at 194°.

Anal. Calcd. for $C_{19}H_{15}Cl_3Si$: Si, 7.45. Found: Si, 7.66.

***n*-Dodecyltris-(*p*-chlorophenyl)-silane.**—To 15.2 g. (0.05 mole) of *n*-dodecyltrichlorosilane[19] in 50 ml. of ether was added an excess of *p*-chlorophenyllithium prepared from 0.3 mole of *n*-butyllithium and 57.3 g. (0.3 mole) of *p*-chlorobromobenzene. The product was refluxed 4 hours, then the ether was removed, chloroform was added, and the mixture was poured into a dilute HCl solution. The chloroform layer was separated, dried over calcium chloride, and the solvent was removed at reduced pressure on the steam-bath. The residue was distilled at 0.1 mm. to give a small fore-fraction boiling at 48°. The remaining residue did not distil up to 240° at 0.1 mm., but when the dark brown residue was heated in a Hickman molecular still for 8 hours, 17 g. (64.1%) of a viscous straw colored distillate was obtained; d^{22}_{4} 1.106, n^{22}_{D} 1.5679; MR_{D} obs., 157.0; calcd.,[18] 155.3.

Anal. Calcd. for $C_{30}H_{37}Cl_3Si$: Si, 5.28. Found: Si, 5.11.

---

[18] Warrick, This Journal, **68**, 2455 (1946).

[19] Whitmore, *et al.*, *ibid.*, **68**, 475 (1946).

Ames, Iowa Received July 19, 1950

[Contribution from the Noyes Chemical Laboratory, University of Illinois]

Alkylation of Grignard Reagents by Quaternary Ammonium Salts. A Novel Synthesis of 1,3-Dialkylindoles

By H. R. Snyder, E. L. Eliel and R. E. Carnahan[1]

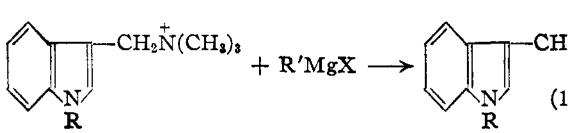
1-Methylgramine methiodide reacts with methylmagnesium iodide and phenylmagnesium bromide to give, in fair yields, 1-methyl-3-ethylindole and 1-methyl-3-benzylindole, respectively. The reaction probably can be applied generally to the synthesis of 1,3-dialkylindoles. Gramine methiodide reacts in the same way to give 3-alkylindoles, but the yields are lower. Other quaternary ammonium salts which have been examined do not alkylate the Grignard reagent in the same way, and methylgramine methiodide apparently does not alkylate phenyllithium or *p*-tolylmercuric chloride. The free bases, 1-methylgramine and gramine, are not satisfactory for the alkylation of Grignard reagents.

In previous reports[2] 1-methylgramine (3-dimethylaminomethyl-1-methylindole) and its methiodide were observed to alkylate various esters containing active methylene or methinyl groups. Carbon alkylation by 1-methylgramine methiodide, and by gramine methiodide as well, now has been extended to include Grignard reagents. 1-Methylgramine methiodide has been found to react with phenylmagnesium bromide to produce 1-methyl-3-benzylindole (Equation 1, R = CH_3, R′ = C_6H_5) in 72.5% yield and with methylmagnesium iodide to produce 1-methyl-3-ethylindole in 43.5% yield. The structure of the last compound, which was previously unknown, was proved by comparison with a sample made by the Fischer synthesis.

---

[1] Minnesota Mining and Manufacturing Company Fellow, 1949–1950.

[2] (a) H. R. Snyder and E. L. Eliel, This Journal, **70**, 3855 (1948); (b) *ibid.*, **71**, 663 (1949).



(1)

1-Alkylindoles are easily accessible from N-alkylanilines *via* the 1-alkyloxindoles.[3,4] Presumably, like 1-methylindole,[5] they can be converted readily to the corresponding gramines by application of the Mannich reaction and thence to 1,3-dialkylindoles by the new reaction of the methiodides. The process appears to be somewhat simpler than previous methods[6] for 1,3-dialkylindoles.

Gramine methiodide reacts similarly with Grignard reagents, but the yields of 3-alkylindoles are not high. With phenylmagnesium bromide it gave 31.5% of 3-benzylindole (Equation 1, R = H, R′ = C_6H_5), with methylmagnesium iodide 15% of 3-ethylindole (R = H, R′ = CH_3), and with benzylmagnesium chloride 13.5% of 3-β-phenethylindole (R = H, R′ = $C_6H_5CH_2$). The structure of the last compound was investigated, since in some reactions[7] benzylmagnesium chloride introduces the *o*-tolyl rather than the benzyl group. The infrared spectrum of the product closely resembled that of 3-benzylindole, and there was no absorption in the region characteristic of an *o*-disubstituted benzene ring. Permanganate oxidation of the product yielded only benzoic acid. Thus a structure containing the *o*-tolyl group is untenable.

A by-product of the reactions of gramine methiodide with methylmagnesium iodide and with phenylmagnesium bromide had the composition and molecular weight corresponding to the formula $C_{18}H_{16}N_2$. The substance had two active hydrogen atoms, as determined by the lithium aluminum hydride method,[8,9] and probably has the structure of *sym*-3,3′-diindolylethane. It was not investigated further.

Attempted applications of the reaction to the free amines, 1-methylgramine and gramine, were unsuccessful; only in the case of the reaction of gramine with phenylmagnesium bromide was even a small amount (3.3%) of alkylation product isolated. *o*-Dimethylaminomethylphenol, a phenolic Mannich base somewhat similar to gramine, also failed to alkylate phenylmagnesium bromide. It is already known that tertiary amino ketones of the Mannich base type, for example, β-phenyl-β-tetrahydroisoquinolinylethyl methyl ketone,[10] react with Grignard reagents to give aminocarbinols, the amino group being unaffected. Similarly, 2,2,6-trimethyl-4-piperidone,[11] a secondary aminoketone having a structure of the Mannich base type, reacts with phenylmagnesium bromide to give an aminocarbinol. Nevertheless, one example of the alkylation of a Grignard reagent by a tertiary amine has been reported; N,N′-benzaldipiperidine reacts with benzylmagnesium chloride to produce N-(1,2-diphenylethyl)-piperidine in 18.5% yield.[12] The present observations suggest that the monomethiodide of the benzaldipiperidine should react more satisfactorily; however, attempts to prepare this reagent were unsuccessful.

Two simple quaternary ammonium salts, benzyltrimethylammonium iodide and benzylpyridinium chloride, failed to alkylate phenylmagnesium bromide. The first reagent evidently brought about the coupling of the Grignard reagent; biphenyl was isolated in approximately 25% yield. Quaternary salts of the quinoline and isoquinoline series are known to react in a different way with the Grignard reagent[13]; for example, quinoline methiodide and phenylmagnesium bromide yield 1-methyl-2-phenyl-1,2-dihydroquinoline. The corresponding reaction occurred, if at all, in the experiment with benzylpyridinium chloride mentioned above only to a minor extent. The methiodide of 2-dimethylaminomethylpyrrole alkylates active methylene compounds readily[14] and in this respect resembles the methiodide of gramine. However, attempts to alkylate a Grignard reagent with this salt were unsuccessful.

Only two organometallic compounds other than Grignard reagents were tested. These reagents, phenyllithium and *p*-tolylmercuric chloride, did not give any dialkylindole in attempted reactions with 1-methylgramine methiodide.

Experimental[15,16]

Reaction of 1-Methylgramine Methiodide with Phenylmagnesium Bromide; 1-Methyl-3-benzylindole.—The Grignard reagent from 0.1 mole of bromobenzene was prepared in ether and this solvent was displaced with 80 ml. of *n*-butyl ether under a current of nitrogen. The resulting solution was stirred with 13.2 g. (0.04 mole) of 1-methylgramine methiodide, at the temperature of the steam-bath and under a current of nitrogen, for 65 hours. The cooled mixture was poured into 100 ml. of 1 *N* HCl. After decomposition of the complex the layers were separated and an ether extract of the acid layer was combined with the organic solution. The solution was washed with 1 *N* HCl, water, aqueous sodium hydroxide, aqueous sodium thiosulfate, and water, and dried over sodium sulfate. Concentration of the solution, finally at the water-pump, left an oil which distilled at 134–137° (0.1 mm.). The light-orange colored distillate solidified on chilling and then melted at 57–60°; it weighed 6.5 g. (72.5%). Two recrystallizations from petroleum ether (b.p. 30–60°) raised the melting point to 60.5–61° (lit.[17] 61°). The picrate crystallized from ethanol as red needles, m.p. 120–121° (lit.[17] 120–121°).

Reaction of 1-Methylgramine Methiodide with Methylmagnesium Iodide; 1-Methyl-3-ethylindole.—The Grignard reagent was prepared from 0.3 mole of methyl iodide. After displacement of the ether by 300 ml. of *n*-butyl ether, 33 g. (0.1 mole) of finely powdered methylgramine methio-

---

[3] R. Stolle, *J. prakt. Chem.*, **128**, 1 (1930).

[4] P. L. Julian and H. C. Printy, THIS JOURNAL, **71**, 3206 (1949).

[5] H. R. Snyder and E. L. Eliel, *ibid.*, **70**, 1703 (1948).

[6] L. Marion and C. W. Oldfield, *Can. J. Research*, **25B**, 1 (1947); A. F. Crowther, F. G. Mann and D. Purdie, *J. Chem. Soc.*, 58 (1943); P. E. Verkade, J. Lieste and W. Meerburg, *Rec. trav. chim.*, **65**, 897 (1946); E. F. J. Janetsky, P. E. Verkade and J. Lieste, *ibid.*, **65**, 193 (1946).

[7] H. Gilman and J. E. Kirby, THIS JOURNAL, **54**, 345 (1932).

[8] J. A. Krynitsky, J. E. Johnson and H. W. Carhart, *ibid.*, **70**, 486 (1948).

[9] F. A. Hochstein and W. G. Brown, Abstracts of the 113th Meeting of the American Chemical Society, Chicago, Illinois, April, 1948, p. 29L.

[10] N. H. Cromwell and J. S. Burch, THIS JOURNAL, **66**, 872 (1944).

[11] G. M. Badger, J. W. Cook and G. M. S. Donald, *J. Chem. Soc.*, 197 (1950).

[12] L. H. Goodson and H. Christopher, THIS JOURNAL, **72**, 358 (1950).

[13] M. Freund, *Ber.*, **37**, 4666, 4679 (1904); **42**, 1101, 1746 (1909).

[14] W. Herz, K. Dittmer and S. J. Cristol, THIS JOURNAL, **69**, 1698 (1947); **70**, 504 (1948).

[15] All melting points are corrected.

[16] Microanalyses by Miss Emily Davis, Miss Rachel Kopel, Mrs. Jane Wood, Mr. Howard Clark and Mr. M. Dare.

[17] P. L. Julian and J. Pikl, THIS JOURNAL, **55**, 2105 (1933).

dide was added to the solution and the resultant suspension was refluxed under nitrogen with intermittent stirring for 19.5 hours. It was then poured onto ice and hydrochloric acid, stirred with sodium bisulfite and filtered to remove some solid material. This solid was stirred twice more with ether and 6 *N* HCl and in each case the extracts were recovered by filtration. After the second acid treatment, only some tarry material remained undissolved. The combined filtrates were separated into layers, the aqueous layer was extracted with ether and then discarded. The ether layers were washed with 1 *N* HCl, water, aqueous sodium carbonate, combined and dried over anhydrous potassium carbonate. Concentration of the solution, finally at the water-pump, left a fluorescent oil which distilled at 96–97° (0.6 mm.) and weighed 6.9 g. (43.5%). An appreciable amount of tarry residue was left in the distilling flask.

The picrate crystallized from alcohol in red needles melting at 96–97° and did not depress the melting point of an authentic sample (see below). It showed a considerable tendency to dissociate into its components.

Anal. Calcd. for $C_{17}H_{16}N_4O_7$: C, 52.59; H, 4.15. Found: C, 52.06; H, 4.23.

1-Methyl-3-ethylindole from Butyraldehyde Methylphenylhydrazone.—The method of Snyder and Smith[18] was used. Six grams (0.050 mole) of *unsym*-methylphenylhydrazine was added to 3.7 g. (0.052 mole) of *n*-butyraldehyde with swirling and cooling in a water-bath. After the exothermic reaction had subsided the mixture was allowed to stand at room temperature for 1 hour. Droplets of water separated. The organic material was taken up in ether (30 ml.) and, after separation of the water, the ether layer was washed with 0.5 *N* HCl, sodium bicarbonate solution and water, dried over sodium sulfate and concentrated. The oily residue was distilled at 0.25 mm., the main fraction (6.1 g., 70%) being collected at 83–85°. A middle cut of this fraction which had $n^{20}D$ 1.5678 was submitted for analysis.

Anal. Calcd. for $C_{11}H_{16}N_2$: C, 74.95; H, 9.15. Found: C, 74.67; H, 9.06.

Six grams of the above hydrazone was dissolved in 9 ml. of glacial acetic acid in a flask equipped with a reflux condenser, and 4.4 g. of boron trifluoride etherate was added through the condenser with swirling. A violently exothermic reaction took place resulting in the loss of some material, and the ammonia-boron trifluoride complex precipitated. After 20 minutes heating on the steam-bath, the mixture was poured into 50 ml. of water and extracted twice with 30 ml. of ether. The combined ether extracts were washed with sodium carbonate, dried over anhydrous potassium carbonate and concentrated. Distillation of the residue yielded 4.1 g. (74%) of a fraction boiling at 65–77° (0.5 mm.). It was redistilled and a middle cut ($n^{20}D$ 1.5806) submitted for analysis.

Anal. Calcd. for $C_{11}H_{13}N$: C, 82.97; H, 8.23. Found: C, 82.74; H, 8.50.

The picrate formed red needles from alcohol, m.p. 97–98°.

Reaction of Gramine Methiodide with Phenylmagnesium Bromide; 3-Benzylindole.—The reaction was carried out as above with 31.6 g. of gramine methiodide and the Grignard reagent from 39.4 g. of bromobenzene in about 200 ml. of *n*-butyl ether. When the reagents were mixed and the mixture was heated to reflux the solid agglomerated on the stirrer and interfered with its action. The temperature was reduced to 100° and after 2 hours the solid mass had disintegrated. The temperature was then increased to 120° for 22 hours, and the mixture finally was refluxed for 17 hours. Trimethylamine was evolved throughout the heating period.

Hydrolysis of the cooled reaction mixture with 1 *N* HCl failed to cause complete dissolution of all the solids. The mixture was filtered and the insoluble portion was treated with ether and 3 *N* HCl. Only a small amount of solid (0.69 g.) survived this treatment. The aqueous layers were combined and extracted with ether. The ether extract was added to the combined organic layers, which were then washed as above and concentrated first at atmospheric pressure and then at the water-pump. The residue was shaken with about 30 ml. of benzene. Filtration yielded 1.72 g. of a crystalline solid melting at 156–158.5°. Recrystallization from 95% ethanol raised the melting point to 168.5°; this material may be *sym*-3,3′-diindolylethane.

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.05; H, 6.19; N, 10.76; mol. wt., 260; active hydrogen 2.00. Found: C, 82.94; H, 6.03; N, 11.10; mol. wt. (ebulioscopic in benzene) 241, 246; active hydrogen,[8,9,19] 2.04, 2.03.

The residue from the concentration of the filtered benzene extract was subjected to steam distillation and the resulting aqueous distillate and residue were separately extracted with ether. Concentration of the extract from the distillate gave a solid which sublimed at room temperature at 0.55 mm. This material melted at 65.5–66.5°; it was considered to be biphenyl, formed during the preparation of the Grignard reagent; weight 0.6 g. (3.1%). The ether extract of the steam distillation residue was concentrated and the residue was sublimed at 0.3 mm., bath temperature 145°, to give 6.53 g. (31.5%) of 3-benzylindole melting, after recrystallization from high-boiling petroleum ether, at 103–105° (lit. 111°).[20]

Reaction of Gramine Methiodide with Methylmagnesium Iodide; 3-Ethylindole.—The reaction was carried out with 31.6 g. (0.1 mole) of gramine methiodide and the Grignard reagent from 35.5 g. (0.25 mole) of methyl iodide in *n*-butyl ether. When the salt was added to the cool Grignard reagent over a period of about 10 minutes the mixture warmed and foamed considerably. After the reaction had moderated the mixture was stirred on the steam-bath for 114 hours. The cooled mixture was hydrolyzed as in the preceding experiment; again a small amount of solid (0.95 g.) resisted the action of 3 *N* HCl. The ether solutions resulting from the hydrolysis were combined and concentrated, and 3-ethylindole was recovered from the residue by steam distillation. It was purified by distillation (b.p. 94–103° (1 mm.)) and was identified by conversion to the picrate. Both forms (m.p. 121°[20] and m.p. 143°[21]) were obtained. When a solution of the lower-melting picrate in absolute ethanol was seeded with the higher-melting form it was only partially converted to the latter form; the resulting crystals underwent sintering and some decomposition at 120°, but decomposition was not complete until 144°.

When the tarry residue from the steam distillation was extracted with hot benzene 0.35 g. of the coupling product, presumably *sym*-3,3′-diindolylethane, melting at 164.5–165.5° after recrystallization from 95% ethanol, was recovered.

Reaction of Gramine Methiodide with Benzylmagnesium Chloride; 3-(β-Phenethyl)-indole.—The reaction was carried out with 31.6 g. (0.1 mole) of the quaternary salt and the Grignard reagent from 31.6 g. (0.25 mole) of benzyl chloride in *n*-butyl ether as before. The suspended solid assumed a red color after a few hours of refluxing. Refluxing was continued for a total of 48 hours, or until the evolution of trimethylamine had become very feeble. The cooled reaction mixture was hydrolyzed as before; 4.54 g. of solid resisted the action of 3 *N* HCl. The ether solution was yellow in color and had a blue fluorescence. Removal of the ether and steam distillation gave 1.8 g. of bibenzyl, m.p. 50.5–51.5°, identified by mixed melting point. Extraction of the steam distillation residue with benzene did not yield any of the supposed diindolylethane obtained in the preceding experiments. Sublimation of the benzene-soluble material at 0.4 mm., bath temperature 140°, gave 3.00 g. (13.6%) of crude β-(β-phenethyl)-indole. After two recrystallizations from dilute ethanol the melting point was constant at 119–119.5°.

Anal. Calcd. for $C_{16}H_{15}N$: C, 86.83; H, 6.83. Found: C, 86.75; H, 6.72.

One gram of this product was heated with a solution of 3 g. of potassium permanganate in 75 ml. of water. After one-half hour the permanganate was decolorized. An additional 2-g. portion was added; it was decolorized within 15 minutes. A final 1-g. portion of the oxidizing agent required about 30 minutes for decolorization. The solution was filtered, concentrated to about 15 ml., and acidified with 6 *N* sulfuric acid. The benzoic acid which separated was

---

(18) H. R. Snyder and C. W. Smith, This Journal, 65, 2452 (1943).

(19) To make sure that the method is applicable to the NH group of indole compounds the determination was also carried out on pure indole; calcd. active hydrogen, 1.00; found, 1.08, 1.10.

(20) R. H. Cornforth and R. Robinson, *J. Chem. Soc.*, 680 (1942).

(21) A. Pictet and L. Duparc, *Ber.*, 20, 3415 (1887).

collected and recrystallized from water; m.p. 118–120°, mixed m.p. 119.5–120°; yield 0.19 g. (34.4%). An exactly similar oxidation of 1 g. of 3-benzylindole gave 0.20 g. (33.9%) of benzoic acid.

Attempted Reaction of 1-Methylgramine with Methylmagnesium Iodide.—To the Grignard reagent from 3.1 g. of methyl iodide in 10 ml. of ether was added a solution of 3.8 g. of 1-methylgramine in 25 ml. of dry xylene. The reflux condenser attached to the flask was drained to allow the ether to escape, and the resulting xylene suspension was refluxed for 24 hours. Hydrolysis of the mixture, finally with 1:1 hydrochloric acid, caused complete solution of the solids. Addition of ammonia to the acid solution caused the separation of an oil, presumably 1-methylgramine, which was not investigated. The organic solution was concentrated to a very small residue which could not be converted to a picrate.

When the reaction was carried out in ethyl ether no neutral product was obtained and 1-methylgramine, identified as the picrate, was recovered. No pure substance could be isolated when the reaction was carried out in pyridine.

Reaction of Gramine with Phenylmagnesium Bromide.—The reaction was carried out with 10.0 g. (0.0575 mole) of gramine and the Grignard reagent from 0.144 mole of bromobenzene in *n*-butyl ether. The mixture was refluxed for 39 hours, during which time an amine was evolved. After hydrolysis, as described above, the acid layer was treated with ammonium chloride and ammonia to permit the recovery of 2.5 g. (25%) of the gramine, identified by mixed melting point. The organic material obtained by concentration of the *n*-butyl ether solution after the hydrolysis was steam distilled to volatilize about 0.1 g. of crystalline material, presumably biphenyl. The non-volatile portion was collected in benzene, recovered, and sublimed at 0.5 mm., bath temperature 140°. The benzylindole so obtained melted at 107.8–108.3° and weighed 0.39 g. (3.3%).

Attempted Reaction of *o*-Dimethylaminomethylphenol with Phenylmagnesium Bromide.—The reagent was prepared by distillation of the commercial product (Rohm and Haas DMP-10) with collection of the fraction boiling at 62–65° (1 mm.), $n^{20}\mathrm{D}$ 1.5303. Treatment of 22.7 (0.15 mole) of this material with an excess (0.4 mole) of phenylmagnesium bromide in *n*-butyl ether was accompanied by an immediate reaction, presumably that of the phenolic hydroxyl group with the Grignard reagent. Subsequent heating of the reaction mixture, finally under reflux for 24 hours, did not cause the liberation of any volatile amine. The cooled reaction mixture was hydrolyzed with hydrochloric acid and the organic layer was extracted with a second portion of the acid. From the organic layer 0.44 g. (1.4%) of biphenyl and 1.83 g. of phenol, identified as the tribromo derivative, were obtained. Treatment of the acid solutions with ammonia, extraction with ether, concentration, and distillation led to the recovery of 3.24 g. (14.3%) of the *o*-dimethylaminomethylphenol, b.p. 57–58° (0.8 mm.), $n^{20}\mathrm{D}$ 1.5247. When a sample of the redistilled aminophenol used in this experiment was subjected to the extractions employed in this isolation, 14% of it was recovered with b.p. 53–54° (0.8 mm.) and $n^{20}\mathrm{D}$ 1.5252, and phenol was also isolated. Thus it appears that phenol was not produced by reaction with the Grignard reagent, but was originally present as an impurity.

Reactions of Benzyltrimethylammonium Iodide and Benzylpyridinium Chloride with Phenylmagnesium Bromide.—The reaction was carried out with 0.1 mole of the benzyltrimethylammonium salt and 0.25 mole of the Grignard reagent in refluxing *n*-butyl ether over a period of 118 hours. There was no appreciable amine evolution. The organic layer after hydrolysis was dried and distilled to give 4.49 g. of biphenyl, b.p. 139–148° (25 mm.), m.p. and mixed m.p., 67–68.5°. A higher boiling fraction, collected at 100–200° (1 mm.), was oxidized by refluxing for 2 hours with a solution of 3 g. of potassium permanganate and 5 ml. of 10% sodium hydroxide in 75 ml. of water. No benzophenone, as such or as the dinitrophenylhydrazone, could be isolated from the neutral material remaining after the oxidation.

In a similar reaction with benzylpyridinium chloride, carried out in refluxing *n*-butyl ether for about 70 hours, biphenyl was isolated in a yield of only 4.3%. A few milligrams of a crystalline solid, perhaps a dihydropyridine derivative, was isolated by sublimation of the acid-soluble products. No diphenylmethane was found.

Reaction of 2-Dimethylaminomethylpyrrole Methiodide with Methylmagnesium Iodide.—When the reaction was carried out in refluxing *n*-butyl ether trimethylamine was formed; it was collected in a Dry Ice trap and identified as the picrate by mixed melting point. However, no 2-ethylpyrrole was found.

Reactions of 1-Methylgramine Methiodide with Phenyllithium and *p*-Tolylmercuric Chloride.—Modifications of the procedures used in the corresponding reaction with phenylmagnesium bromide were employed, and *n*-butyl ether was used as the solvent. Amine evolution was feeble in the phenyllithium reaction. The amine formed was condensed in a Dry Ice trap and proved as trimethylamine by conversion to the picrate. Evolution of amine from the *p*-tolylmercuric chloride reaction mixture was more copious. Neither reaction mixture gave any 1-methyl-3-benzylindole when subjected to the general procedure used above for the isolation of this product.

URBANA, ILLINOIS RECEIVED SEPTEMBER 11, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Preparation of α-Bromoacetals[1]

BY ELLIOT N. MARVELL AND MICHEAL J. JONCICH

This paper describes a study carried out to find a more suitable brominating agent for acetals than free bromine. It has been shown that acetals can be brominated readily by N-bromosuccinimide (NBS). The predominant products of the treatment of the diethyl acetals of acetaldehyde, propionaldehyde, butyraldehyde and isobutyraldehyde were the α-bromoacetals. A by-product containing a more reactive bromine was noted in each case. An attempt was made to determine whether bromination can occur on the carbon containing the two ether linkages by treating benzaldehyde diethyl acetal with NBS. The sole isolable product was ethyl benzoate. The yields of pure α-bromoacetals suggest that this method is preferable to the use of elementary bromine for the preparation of low molecular weight α-bromoacetals.

Discussion

Although aldehydes can be brominated directly to give α-bromoaldehydes,[2] their preparation is generally carried out by bromination of the acetal followed by hydrolysis to the free aldehyde. Pinner[3] brominated acetals without providing for the removal of the hydrogen bromide generated in the reaction, but later workers have used either suspended calcium carbonate[4] or pyridine[5] to destroy the acid as rapidly as it is formed. It has

---

(1) Published with the approval of the Monograph Publications Committee, Oregon State College, as Research Paper No. 168, School of Science, Department of Chemistry. Presented in part before the Northwest Regional Meeting of the American Chemical Society, at Richland, Washington, June 9, 1950. This article is based on a thesis submitted by M. J. Joncich in partial fulfillment of the requirements for the degree of Master of Science at Oregon State College, June, 1950.

(2) (a) A. Franke, *Ann.*, **351,** 421 (1907); (b) Dworzak and Prodinger, *Monatsh.*, **53/54,** 588 (1929).

(3) Pinner, *Ber.*, **5,** 147 (1872).

(4) E. Fischer and K. Landsteiner, *ibid.*, **25,** 2549 (1892).

(5) S. M. McElvain and P. M. Walters, THIS JOURNAL, **64,** 1963 (1942).