abandoned when it was found that the yield of the nitrodiol from a condensation of pentanedial and nitromethane could not be raised above 3%.

Work on the trifunctional aminocyclanols is to be continued.

Experimental

All m.ps. are corrected. Microanalyses by Mr. R. Pyke.

d,l-1-**Ethoxy-2-chlorocyclohexanol-3**[10,11] (A).—Instead of using chlorine gas, aqueous hypochlorous acid was prepared by acidifying commercial 5 or 12% sodium hypochlorite solution (available at grocery stores). About 0.09 mole of the hypochlorous acid solution was added at 0° in portions to 0.055 mole of 1-ethoxycyclohexene-2.[12] After the last portion was added the mixture was stirred one hour longer at 0°, and the chlorohydrin was then extracted with benzene. The dried benzene extract was distilled *in vacuo* and the product collected at 110–117° (12 mm.). The crude product was redistilled, giving a 41% yield of colorless liquid, b.p. 98–105° (7.5 mm.), n^{21}_{D} 1.4839 (reported[3] n^{25}_{D} 1.4817, 1.4810).

(B).—The procedure was carried out with an N-chlorourea solution, according to the general procedure of Detoeuf,[13] giving the product in 35% yield.

d,l-1-**Ethoxy-2,3-epoxycyclohexane**[10,14] (A).—Treatment of the chlorohydrin with a dry ethereal suspension of powdered sodium hydroxide gave a 26% yield of colorless liquid, b.p. 74–77° (7 mm.). The procedure was like that used by Brunel[4] on the iodohydrin.

(B).—The chlorohydrin was treated with aqueous sodium hydroxide. The procedure was like that which had been used by Osterberg[15] on 2-chlorocyclohexanol. The yield was 23%.

(C).—Treatment of 1-ethoxycyclohexene-2[12] (b.p. 55–60° (12–15 mm.)) with perbenzoic acid by the procedure of Mousseron, *et al.*,[3] gave a 70% yield of the epoxide, b.p. 79–82° (15–16 mm.), n^{25}_{D} 1.4530 (reported[3] 1.4493).

d,l-**3-Amino-1-ethoxycyclohexanol-2.**[16,17]—A solution of 2.0 g. of the ethoxy-epoxide in 25 ml. of ethanol (saturated at 25° with dry ammonia) was heated in a sealed tube for six hours at 120°. Ethanol and ammonia were then removed by vacuum distillation and the residue washed well with petroleum ether (60–70°). The residue was sublimed under vacuum and recrystallized thrice from benzene–petroleum ether (1:9). The yield of colorless crystals, m.p. 132–134°, was 0.35 g. (16%).

Anal. Calcd. for $C_8H_{17}NO_2$: neut. equiv., 159. Found: neut. equiv., 158.

Variations of temperature or time did not improve the above yield. The aminediol was characterized by conversion to the derivatives below.

d,l-**3-*p*-Nitrobenzoylamino-1-ethoxycyclohexanol-2.**[16,17]—An acylation procedure similar to that of Leffler and Adams[18] gave a 60% yield of colorless needles, which after recrystallization from 20% ethanol melted at 201–203° (dec.).

Anal. Calcd. for $C_{15}H_{20}N_2O_5$: C, 58.43; H, 6.54; N, 9.09. Found: C, 58.54; H, 6.80; N, 8.99.

d,l-**3-Aminocyclohexanediol-1,2 Hydrobromide.**[16,17]—A 5.0-g. portion of the aminediol monoethyl ether was boiled under reflux for 90 minutes with 23 ml. of 47% aqueous hydrobromic acid. The solution was vacuum distilled to dryness. Water (100 ml.) was added, and the resulting solution again distilled to dryness. Finally, 250 ml. of water was added, the mixture refluxed for two hours, and again distilled to dryness.

The gummy residue was taken up in a minimum volume of boiling ethanol–benzene (2:3), and pure benzene was added until crystals separated. The crude product (m.p. 150–170°) was recrystallized in a similar manner, giving 2.67 g. (40%) of crystalline hydrobromide, m.p. 167–168°.

Anal. Calcd. for $C_6H_{14}BrNO_2$: C, 33.97; H, 6.65; N, 6.61. Found: C, 33.78; H, 7.03; N, 6.72.

d,l-**3-*p*-Nitrobenzoylaminocyclohexanediol-1,2.**[16,17]—Acylation of the neutralized hydrobromide with *p*-nitrobenzoyl chloride as above gave a 49% yield of colorless plates. After two recrystallizations from 20% ethanol the compound melted at 182–183° (dec.) when heated rapidly.

Anal. Calcd. for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.75; N, 10.00. Found: C, 55.46; H, 6.30; N, 9.50.

Oxidation of the Nitrobenzoylaminocyclohexanediol with Periodic Acid.—An 18.3-mg. sample of the *p*-nitrobenzoylaminocyclohexanediol was treated with 2.72 ml. of 18.4 millimolar aqueous paraperiodic acid at 25° with stirring. Iodometric titrations with sodium arsenite revealed that 0.95–0.97 mole of periodic acid per mole of acylaminediol had been consumed within 20–30 minutes.

2-Nitrocyclohexanediol-1,3.[16]—A 1.5-g. portion of pentanedial[19] and equimolar quantities of nitromethane and 10% aqueous sodium hydroxide solution were allowed to react. The reaction mixture was neutralized, vacuum distilled, and the product obtained from the residue by ether extraction. The best yield obtained was only 3%. The product gave negative Schiff and Fehling tests for free aldehyde groups, and melted at 139–142°; analysis indicated it is not entirely pure. The configuration is not known; three diastereomers are possible.

Anal. Calcd. for $C_6H_{11}NO_4$: C, 44.72; H, 6.83; N, 8.70. Found: C, 44.76; H, 7.11; N, 9.76.

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[10] The homogeneity of this product is not well established.

[11] Of four possible diastereomeric configurations for this product, only the configurations (1,2-*cis*) and (1,3-*cis*) are probable. On the basis of the limited evidence now available we consider the configuration (1,2-*cis*) more probable.

[12] F. Hoffman and P. Damm, *Chem. Zentr.*, **97**, I, 2342 (1926).

[13] A. Detoeuf, *Bull. soc. chim.*, [4] **31**, 102 (1922); J. A McRae, E. H. Charlesworth and D. S. Alexander, *Can. J. Research*, **21B**, 5 (1943).

[14] Of four possible diastereomeric configurations for this product, only the configurations (2,3-*cis*) and (1,2,3-*cis*) are probable. On the basis of the limited evidence now available we consider the configuration (2,3-*cis*) more probable.

[15] A. E. Osterberg, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 185.

[16] It is believed that this product is homogeneous and consists of a single pure diastereomer.

[17] Of four possible diastereomeric configurations for this product, only the configurations (1,3-*cis*) and (1,2-*cis*) are probable. On the basis of the limited evidence now available we consider the configuration (1,3-*cis*) more probable.

[18] M. T. Leffler and R. Adams, THIS JOURNAL, **59**, 2256 (1937).

[19] The dial was prepared from cyclopentene ozonide (*ibid.*, **65**, 2183 (1943); *Ber.*, **41**, 1705 (1908); or, better, by the cleavage of cyclopentanediol-1,2 with lead tetraacetate (*Ann.*, **518**, 26 (1935)).

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Grignard Preparation of Fluorene-2-Carboxylic Acid[1]

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In connection with work on incorporation of isotopic elements into the fluorene molecule, the preparation of a Grignard reagent from 2-bromofluorene was studied. Under certain conditions this was found to be successful and carbonation of the resulting reagent solution furnished the 2-carboxylic acid. The difficulty of forcing a reaction between magnesium and bromo derivatives of polynuclear aromatic hydrocarbons is well recognized. Miller and Bachman[2] did not observe formation of the Grignard reagent from 2-bromofluorene by use of conventional techniques. In the present work, this reagent was obtained in about 20% yields by the reaction of a mixture of 2-bromofluorene and ethyl bromide with magnesium.

This entrainment reaction was carried out at ether reflux temperature and under these conditions

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[1] The work described in this paper was sponsored by the Atomic Energy Commission. It was supported in part by a grant from the Henry, Laura and Irene B. Dernham Fund of the American Cancer Society and the Christine Breon Fund.

[2] H. F. Miller and G. B. Bachman, THIS JOURNAL, **57**, 766 (1935).

little, if any, interaction with the 9-position (methylene group) took place. The identity of the acid formed by carbonation was confirmed by permanganate oxidation of a portion to fluorenone-2-carboxylic acid, both acids having appropriate melting points. The Grignard reaction may furnish a convenient source of small amounts of fluorene-2-carboxylic acid.

Experimental[3]

The 2-bromofluorene was obtained by the method of Thurston and Shriner.[4] The preparation was studied in two ways, varying the time of reaction and the amount of ethyl bromide used.

In the preferred method of reaction, 5 g. of 2-bromofluorene with excess magnesium in 100 ml. of ether were treated dropwise with 20 ml. of ethyl bromide in 100 ml. of ether during one hour. The solution was then refluxed one-half hour and carbonated while still warm with Dry Ice. The mixture was hydrolyzed with dilute hydrochloric acid and the organic layer removed and washed with water. It was extracted with three portions of sodium carbonate solution and the extracts combined and acidified. This caused precipitation of the acid as a cream colored powder. After filtering, washing and drying it weighed 900 mg. (21%). From the filtrate from the acid precipitation, on standing overnight, 50 mg. of a more soluble white acid, m.p. 216–221°, was formed. This was not identified but did not decompose on boiling its alkaline solution or on melting.

The fluorene-2-carboxylic acid was recrystallized from acetone–water and from ether, m.p. 260–267° with some sublimation and darkening. The ether solution was decolorized with charcoal and the acid crystallized again by concentrating the solution. This gave a product m.p. 275–277° with sublimation, on rapid heating. Schiessler and Eldred[5] list 265–274° with decomposition as the m.p. of the acid obtained by one method and 271–275° without decomposition as the m.p. of the acid formed by another process.

In this Grignard synthesis, all of the aryl bromide was initially present and maximum utilization of the entraining action of ethyl bromide was achieved. The large excess of ethyl bromide was employed to improve the yield further if possible. Some of the unreacted 2-bromofluorene may be recovered from the neutral reaction products.

The second method of carrying out the reaction employed less ethyl bromide and the mixture was refluxed overnight. A mixture of 0.5 g. of 2-bromofluorene with 0.5 ml. of ethyl bromide in 50 ml. of ether reacted with excess magnesium (about 5 g.) until the action was slow. A solution of 4.5 g. of 2-bromofluorene and 1.5 ml. of ethyl bromide in 100 ml. of ether was then added slowly during one-half hour. Twenty ml. of benzene was also added during this time. The resulting orange-brown solution was refluxed overnight (16.5 hours) and carbonated. The mixture was hydrolyzed and the acid isolated as before. The yield was 750 mg. or 17.5%.

A portion of the fluorene-2-carboxylic acid was oxidized in aqueous alkaline solution by an excess of permanganate by heating several hours on the steam-bath. The excess of permanganate was destroyed by oxalic acid, and the solution filtered. Acidification of the filtrate furnished the fluorenone-2-carboxylic acid which formed yellow crystals from ether. It had m.p. about 330° with much sublimation and some decomposition. Schiessler and Eldred[5] give 333–335° with decomposition as the m.p. of fluorenone-2-carboxylic acid.

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[3] Melting points are uncorrected.

[4] J. T. Thurston and R. L. Shriner, THIS JOURNAL, **57**, 2163 (1935).

[5] R. W. Schiessler and N. R. Eldred, *ibid.*, **70**, 3958 (1948).

Arylsulfonic Esters of Bromophenols in Grignard Preparations[1]

BY D. C. MORRISON

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The work of Gilman and others[2] on reactions of aryl esters of arylsulfonic acids with Grignard reagents showed that only slight action took place at 35°. During the course of work on Grignard preparations, the possibility of obtaining a reaction of magnesium with bromophenyl esters of aromatic sulfonic acids was examined. It was hoped to use these bromophenol esters as aryl halides and obtain protection of the phenolic group by this esterification.

Some of the bromophenyl esters reacted successfully under entrainment conditions giving about 25% yields of the desired Grignard reagent ($Ar{\cdot}SO_2{\cdot}O{\cdot}C_6H_4{\cdot}MgX$) whose presence was proved by carbonation and isolation of the corresponding acid. The latter and other reaction products of these Grignard reagents could be hydrolyzed, removing the sulfonate group and forming the corresponding hydroxy derivatives.

Bromoalkyl esters of arylsulfonic acids would not be expected to function as alkyl halides in a similar reaction as alkyl esters of these acids have labile alkyl groups.

p-Bromophenol was used in most of the work and its esters with benzene- and toluenesulfonic acids were studied. These reacted difficultly or not at all with magnesium alone but more facile reaction occurred if the ester bromide was entrained with excess ethyl bromide. Carbonation with Dry Ice and isolation of the acids in the usual manner furnished the arylsulfonic esters of *p*-hydroxybenzoic acid ($Ar{\cdot}SO_2{\cdot}O{\cdot}C_6H_4{\cdot}COOH$). The tosyl ester was hydrolyzed to *p*-hydroxybenzoic acid.

This type of Grignard reaction is apparently not general, as esters of several other bromophenols gave little or none of the desired carboxylic acids or unknown substances. Thus, the ester of *o*-bromophenol yielded a product different from the known desired acid (arylsulfonate of salicylic acid) and which was not identified. The phenyl ester of *p*-bromobenzenesulfonic acid, entrained with ethyl bromide and carbonated, gave two acids according to the conditions. These were not further examined.

As the hydroxy derivatives ultimately desired were organophosphorus acids with a *p*-hydroxy group, the reaction of the *p*-bromophenyl ester Grignards with $POCl_3$ was examined. This reaction was carried out in accordance with the directions of Kosolapoff[3] who has demonstrated that, under suitable conditions, phosphinic acids (R_2-POOH) can be prepared by this method. The expected product was the bis-(arylsulfonate) of di-(*p*-hydroxyphenyl)-phosphinic acid. However,

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[1] The work described in this paper was sponsored by the Atomic Energy Commission. It was supported in part by a grant from the Henry, Laura and Irene B. Dernham Fund of the American Cancer Society and the Christine Breon Fund.

[2] H. Gilman, N. J. Beaber and C. H. Myers, THIS JOURNAL, **47**, 2047 (1925).

[3] G. M. Kosolapoff, *ibid.*, **64**, 2982 (1942).