mole) and ethyl 5-nitro-2-furimidate hydrochloride (6.6 g, 0.03 mole) in methanol (20 ml, previously dried by distillation from sodium methoxide–diethyl oxalate) was warmed for 1 hr. Dilution with hot water (15 ml) induced crystallization of small yellow prisms (6.0 g, 81%) mp 230–231° (lit.[8] mp 224–226°). The product ran as a single spot on alumina developed with benzene.

The other benzimidazoles were prepared similarly, as yellow to orange crystalline solids. In many cases they crystallized directly from the methanol. All products were examined by thin layer chromatography on alumina and purified until they ran as a single spot.

2-(5-Nitro-2-furyl)benzoxazole crystallized from DMF–methanol as yellow needles (63%), mp 231–232° (lit.[8] mp 225–227°).

New Compounds

The Synthesis of Tertiary Arylalkylamines from Aryl Grignard Reagents

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The arylalkyl tertiary amines are an important class of compounds in medicinal chemistry which contain drugs effective as antihistamines, spasmolytics, tranquilizers, and antidepressants. We now report that the reaction of aryl Grignard reagents with dialkylaminoalkyl chlorides provides a useful general procedure for the synthesis of arylalkylamines. The method is exemplified with phenyl, 1-naphthyl, 9-phenanthryl, 3-indenyl, and 3-benzo[*b*]thienylmagnesium bromides. It is also applicable to indole,[1] 2,5-diphenylfuran,[2] and 3-phenylindene.[3] A similar use of aryllithium compounds is illustrated by 2-benzo[*b*]-thienyllithium.

Experimental Section[4]

N,N-Dimethylphenethylamine Hydrochloride.—A dry solution of 2-dimethylamino-1-chloroethane (0.2 mole)[5] in toluene (100 ml) was added to the Grignard reagent from bromobenzene (32 g, 0.2 mole) in ether (100 ml). The mixture was heated under reflux for 1 hr and then poured onto ice and an excess of HCl. The aqueous layer was separated off, washed with toluene, then made alkaline with NaOH, and extracted with ether. Evaporation of the dried ethereal extracts left the amine as an oil (7.2 g) which was converted into its hydrochloride. The latter was crystallized from 2-propanol–ether mixture to yield 5.0 g (13.4%) of colorless needles, mp 166–167°, lit.[6] mp 171°.

Anal. Calcd for $C_{10}H_{16}ClN$: C, 64.8; H, 8.7; N, 7.5. Found: C, 64.5; H, 8.4; N, 7.5.

N,N-Dimethyl-3-phenylpropylamine hydrochloride was prepared similarly from phenylmagnesium bromide (0.2 mole) and 3-dimethylamino-1-chloropropane (0.4 mole). It was crystallized from 2-propanol–ether mixture and obtained in 13% yield (5.2 g). The hydrochloride was extremely hygroscopic and the product was characterized by its **hydrogen oxalate,** mp 131–133° (from ethyl methyl ketone), and **picrate,** mp 96–98°, lit.[7] mp 99°.

Anal. Calcd for $C_{11}H_{17}N \cdot C_2H_2O_4$: C, 61.6; H, 7.6; N, 5.5. Found: C, 61.9; H, 7.8; N, 5.5.

Anal. Calcd for $C_{11}H_{17}N \cdot C_6H_3N_3O_7$: C, 52.0; H, 5.1; N, 14.3. Found: C, 52.2; H, 5.0; N, 14.1.

N,N-Dimethyl-2-(9-phenanthryl)ethylamine Hydrochloride.—In a similar manner 2-dimethylamino-1-chloroethane (0.05 mole) in toluene (50 ml) was added to the Grignard reagent from 9-bromophenanthrene (12.9 g, 0.05 mole) in ether–benzene (30:30 ml) and the stirred mixture was heated under reflux for 2 hr. The hydrochloride, after crystallization from 2-propanol–ether mixture, yielded 1.5 g (10.5%) of colorless needles, mp 228–230°.

Anal. Calcd for $C_{18}H_{20}ClN$: C, 75.6; H, 7.1; N, 4.9. Found: C, 75.7; H, 7.3; N, 4.6.

N,N-Dimethyl-3-(9-phenanthryl)propylamine hydrochloride was prepared similarly from 9-phenanthrylmagnesium bromide (0.05 mole) and 3-dimethylamino-1-chloropropane (0.05 mole). It was obtained in 7.3% yield (1.1 g) as colorless needles (from 2-propanol–ether), mp 220–222°.

Anal. Calcd for $C_{19}H_{22}ClN$: C, 76.2; H, 7.4; N, 4.7. Found: C, 76.4; H, 7.3; N, 4.6.

N,N-Dimethyl-2-(1-naphthyl)ethylamine Hydrochloride.—A dry solution of 2-dimethylamino-1-chloroethane (0.5 mole) in toluene (150 ml) was added slowly, during 90 min, to the Grignard reagent from 1-bromonaphthalene (52 g, 0.25 mole) in ether–benzene (150:150 ml); the reaction was sufficiently exothermic to maintain reflux without additional heating. The mixture was stirred overnight at room temperature in an atmosphere of nitrogen and then worked up to afford 4.1 g of the amine, as an oil, which was converted into its hydrochloride. The latter was crystallized first from ethanol–ether mixture and then from ethanol to yield 2.5 g (4.2%) of colorless microcrystalline needles, mp 214–215°, lit.[8] mp 213°.

Anal. Calcd for $C_{14}H_{18}ClN$: C, 71.3; H, 7.7; N, 5.9. Found: C, 71.1; H, 7.4; N, 5.9.

N,N-Dimethyl-2-(3-indenyl)ethylamine Hydrochloride.—Ethylmagnesium bromide (1.0 mole) was prepared in diethyl ether (200 ml) and the solvent was then displaced by dry toluene (700 ml). A solution of indene (116 g, 1.0 mole) in toluene (100 ml) was added dropwise during 1 hr to the stirred mixture at 95° in an atmosphere of nitrogen, and the temperature was maintained at 95–100° for a further 10 hr. After being cooled to room temperature the solvent was decanted from the pale yellow solid indenyl Grignard reagent[9] and the latter was then washed with two 200-ml portions of dry toluene and suspended in anhydrous ether (700 ml). To this suspension was added a dry solution of 2-dimethylaminoethyl-1-chloroethane (1.0 mole) in ether (500 ml) during 30 min. The reaction was sufficiently exothermic to maintain reflux without additional heating and after a further 2 hr the mixture was poured onto crushed ice and aqueous NH_4Cl. The oily amine (99.9 g) was isolated and converted into its hydrochloride which, after being crystallized from 2-propanol, was obtained as colorless needles (79.4 g, 35.6%), mp 175–177.5°.

Anal. Calcd for $C_{13}H_{18}ClN$: C, 69.8; H, 8.1; N, 6.3. Found: C, 69.6; H, 8.1; N, 6.5.

N,N-Dimethyl-2-(3-benzo[*b*]thienyl)ethylamine Hydrogen Oxalate.—A dry solution of 2-dimethylaminoethyl-1-chloroethane (0.2 mole) in toluene (100 ml) was added to 3-benzo[*b*]-thienylmagnesium bromide[10] [from 21.3 g (0.1 mole) of 3-bromo-

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(4) Melting points were recorded using an Electrothermal® melting point apparatus comprising a gas-heated block and a thermometer calibrated for stem exposure. Microanalyses are by Mr. M. J. Graham (Smith Kline and French Laboratories Ltd.). The purity and identity of all products were confirmed by thin layer chromatography, and ultraviolet and infrared absorption spectra.
(5) The molarity of the dimethylaminoalkyl chloride reagent, used in all of the experiments, refers to the quantity of the corresponding hydrochloride which was neutralized with 40% NaOH and extracted three times with toluene. The toluene extracts were dried twice (KOH).
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benzo[*b*]thiophene[11]] in ether–benzene (50:50 ml) with cooling to maintain the temperature below 25°. The mixture was stirred in an atmosphere of nitrogen and heated under reflux for 4 hr and then poured onto cold aqueous NH_4Cl. The oily amine (1.7 g) was isolated, but since its hydrochloride could not be crystallized, the product was characterized as its hydrogen oxalate. The latter was prepared in ethanol and recrystallized from methanol to furnish 1.1 g (4%) of colorless needles, mp 179–181° dec.

Anal. Calcd for $C_{12}H_{15}NS \cdot C_2H_2O_4$: C, 56.9; H, 5.8; N, 4.7. Found: C, 57.1; H, 5.8; N, 4.9.

N,N-Dimethyl-2-(2-benzo[*b*]thienyl)ethylamine Hydrochloride.—A dry solution of 2-dimethylaminoethyl-1-chloroethane (0.2 mole) in toluene (100 ml) was added to 2-benzo[*b*]thienyllithium[12] [prepared from 13.7 g (0.1 mole) of benzo[*b*]thiophene and 0.2 mole of butyllithium] in ether (140 ml) at 10°. The mixture was stirred in an atmosphere of nitrogen and heated under reflux for 6 hr and then poured onto crushed ice. The amine (8.0 g of oil) was isolated and converted into its hydrochloride. Crystallization of the latter from 2-propanol yielded 4.9 g (20%) of colorless needles, mp 227–229°.

Anal. Calcd for $C_{12}H_{16}ClNS$: C, 59.6; H, 6.7; N, 5.8. Found: C, 59.5; H, 6.9; N, 5.7.

A pure sample of the **amine**, obtained by neutralization of the hydrochloride, was crystallized from pentane as colorless needles, mp 39–41°.

Anal. Calcd for $C_{12}H_{15}NS$: C, 70.2; H, 7.4; N, 6.8. Found: C, 70.3; H, 7.5; N, 6.6.

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D-Arabinose and 2-Deoxy-D-ribose Derivatives

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In a program directed toward nucleoside synthesis a number of derivatives of D-arabinose and 2-deoxy-D-ribose were synthesized. A few of these were new compounds which seemed worth recording in the chemical literature. These compounds were ethyl 2,3,5-tri-*O*-benzyl-D-thioarabinoside (I), 2,3,5-tri-*O*-benzyl-D-arabinose diethyl mercaptal (II), 2,3,5-tri-*O*-benzyl-4-*O*-acetyl-D-arabinose diethyl mercaptal (III), 5-*O*-trityl-2,3,4-tri-*O*-benzoyl-D-arabinose (IV), and 5-*O*-trityl-2-deoxy-D-ribose ethylene mercaptal (V).

Treatment of 2,3,5-tri-*O*-benzyl-β-D-arabinose with ethyl mercaptan and aqueous HCl[1] gave I. More vigorous conditions formed II. Oxidation[2] of 5-*O*-trityl-2,3,4-tri-*O*-benzoyl-D-arabinose diethyl mercaptal[3] with HgO–$HgCl_2$ gave IV. 2-Deoxy-D-ribose ethylene mercaptal[4] was converted to V by reaction with trityl chloride in pyridine.[2]

Experimental Section[5]

Ethyl 2,3,5-Tri-*O*-benzyl-D-thioarabinoside (I).—2,3,5-Tri-*O*-benzyl-β-D-arabinofuranose (4.2 g, 0.01 mole), 1.24 g (0.02 mole) of ethyl mercaptan, and 1 ml of concentrated HCl were mixed and macerated with a glass rod until a homogeneous paste was achieved. The mixture was refrigerated overnight. About 2.5 ml of water was added, and the mixture was extracted with 5 ml of $CHCl_3$. The $CHCl_3$ extract was dried ($MgSO_4$), filtered, and evaporated to dryness under reduced pressure, yield 3.45 g. The product was chromatographed on 100 g of Woelm neutral alumina (3% water) packed in benzene. The column was eluted with C_6H_6–$CHCl_3$ (8:2) collecting fifty 10-ml fractions. Fractions 9–30 were combined and evaporated to dryness under reduced pressure. The product was a clear oil (2.5 g, 54%). Thin layer chromatography [silica gel; C_6H_6–CH_3OH (95:5)] gave a single spot with R_f 0.49. The infrared spectrum (neat) had bands at 3000, 2820, 1490, 1445, 1355, 1250, 1195, 1105, 1035, 975, 905, 734, and 695 cm^{-1}.

Anal. Calcd for $C_{28}H_{32}SO_4$: C, 72.39; H, 6.94; S, 6.90. Found: C, 72.05; H, 6.87; S, 6.64.

2,3,5-Tri-*O*-benzyl-D-arabinose Diethyl Mercaptal (II).—A mixture of 4.2 g (0.01 mole) of 2,3,5-tri-*O*-benzyl-β-D-arabinofuranose, 1 ml of concentrated H_2SO_4, and 50 ml of ethyl mercaptan was stirred vigorously under anhydrous conditions overnight. Chloroform (50 ml) and 50 ml of water were added to the reaction mixture. The $CHCl_3$ layer was removed and extracted successively with 50 ml of 2.0 *N* NaOH solution, 50 ml of saturated $NaHCO_3$ solution, and 50 ml of water. The $CHCl_3$ solution was filtered, and the filtrate was evaporated to dryness under reduced pressure to give an oil (5.19 g). The product was chromatographed on the same system as in the previous experiment but using 200 g of alumina. Elution was done with 200 ml of C_6H_6–$CHCl_3$ (9:1), 250 ml of C_6H_6–$CHCl_3$ (8:2), and C_6H_6–$CHCl_3$–CH_3OH (78:20:2), collecting one hundred 10-ml fractions. Fractions 68–78 were combined and concentrated under reduced pressure to give 1.15 g of a pale yellow oil. The R_f value [silica gel; C_6H_6–CH_3OH (99:1)] was 0.43. The infrared spectrum had bands at 3495, 2810, 1475, 1440, 1385, 1335, 1250, 1200, 1085, 1025, 905, 734, and 697 cm^{-1}.

Anal. Calcd for $C_{30}H_{38}S_2O_4$: C, 68.40; H, 7.27; S, 12.17; O, 12.15. Found: C, 68.12; H, 7.45; S, 12.11; O, 12.11.

2,3,5-Tri-*O*-benzyl-4-*O*-acetyl-D-arabinose Diethyl Mercaptal (III).—A solution of 6.5 g (0.012 mole) of 2,3,5-tri-*O*-benzyl-D-arabinose diethyl mercaptal and 12 ml of acetic anhydride in 90 ml of anhydrous pyridine was allowed to stand at room temperature overnight. The solution was poured into a vigorously stirred mixture of 200 g of ice and 200 ml of $CHCl_3$. The resulting mixture was allowed to stand until the ice had melted. The $CHCl_3$ layer was removed and extracted with three 100-ml portions of ice-cold 3 *M* $NaHSO_4$ solution, two 150-ml portions of saturated $NaHCO_3$ solution, and 150 ml of water. The $CHCl_3$ solution was filtered through paper, and the solvent was removed from the filtrate by evaporation under reduced pressure. The residue was a pale amber oil (6.9 g, 99%). Thin layer chromatography [silica gel; C_6H_6–C_6H_{12}–CH_3OH (50:47:3)] showed a single spot with R_f 0.62. The infrared spectrum (neat) had no absorption in the hydroxyl region but had a strong band at 1730 cm^{-1} (ester). Other infrared bands were at 2980, 2900, 2820, 1460, 1440, 1362, 1230, 1090, 1085, 1025, 965, 907, 750, 733, and 695 cm^{-1}.

Anal. Calcd for $C_{32}H_{40}S_2O_5$: C, 67.57; H, 7.09; S, 11.27; O, 14.08. Found: C, 67.17; H, 7.17; S, 10.90; O, 14.06.

5-*O*-Trityl-2,3,4-tri-*O*-benzoyl-D-arabinose (IV).—A mixture of 29.95 g (0.037 mole) of 5-*O*-trityl-2,3,4-tri-*O*-benzoyl-D-arabinose diethyl mercaptal, 35 g of yellow HgO, 40 g of $HgCl_2$, 25 ml of water, and 375 ml of acetone was stirred at room temperature overnight. The mixture was filtered, and the filter cake was washed thoroughly with acetone. The combined filtrate and washings were evaporated to dryness under reduced pressure. The residue was partitioned between 200 ml of water and 200 ml of $CHCl_3$. The phases were separated, and the aqueous phase was extracted with 50 ml of $CHCl_3$ which was combined with the previous $CHCl_3$ phase. The $CHCl_3$ solution was washed with three 100-ml portions of water, filtered, and evaporated to dryness under reduced pressure to give 23.4 g of residue. A portion (11.6 g) of the residue was crystallized from C_6H_6, and a second fraction was obtained by dilution of the mother liquor with Skellysolve B. The total yield of recrystallized material was 8.6 g. The crystalline material was combined with 2.5 g from another experiment and recrystallized from 50 ml of C_6H_6: 7.17 g, mp 92–93°, $[\alpha]^{25}D$ +46° (*c* 2, $CHCl_3$). The ultraviolet spectrum (C_2H_5OH) had maxima at 229 mμ (ε 36,800), 254 (2950), 260 (2450), 266 (2300), 270 (2300), 273 (2300), and 281 (1850). The infrared spectrum (Nujol mull) had bands at 1725, 1600, 1580, 1490, 1245, 1100, 1090, 1065, 1020, 710, and 700 cm^{-1}. The nmr spectrum in $CDCl_3$ had a multiplet centered at δ 3.57 (2 H on C-5), a multiplet centered at 5.88 (2 H on C-3 and C-4), a doublet of doublets centered at 6.73 (H on C-2), multiple peaks at 7.0–8.28 (aromatic), and a singlet at 9.78 (aldehyde H).

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