material by NMR and optical rotation showed 43% (+)-menth-3-ene ($[\alpha]^{23}{}_{589}$ + 106°, giving 97% optical purity) and 57% (+)-menth-2-ene.

Menthenes from (+)-Neomenthyl Tosylate (6). A solution of 99.0 mg (0.32 mmol) of (+)-neomenthyl tosylate (**6**) in 3 ml of dry ether was stirred over 2.72 g of dehydrated alumina at 0° for 1.5 days. Gas–liquid chromatography (10 ft × 0.25 in., 10% FFAP on Chromosorb W 60/80; using *p*-cymene as added, calibrated, internal standard) showed 91% menthenes (Δ^2 and Δ^3 combined). Careful distillation removed most of the solvent and preparative GLC (20 ft × 0.375 in., 20% QF-1 on Chromosorb W 45/60) afforded a pure sample of the Δ^2- and Δ^3-menthene mixture. Analysis of this material by NMR and optical rotation showed 89% (+)-menth-3-ene ($[\alpha]^{23}{}_{589}$ + 86.1°, giving 74% optical purity) and 11% (+)-menth-2-ene.

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Registry No.—**1**, 57346-50-6; **2**, 35652-87-0; **3**, 2230-82-2; **6**, 2230-77-5; alumina, 1344-28-1; 2-octyl *N,N*-dimethylsulfamate, 57346-51-7; 5α-cholest-2-ene, 570-73-0; 5α-cholestan-3β-yl tosylate, 3381-52-0; 4-benzoyloxycyclohexene, 36978-27-5; *trans*-4-benzoyloxycyclohexyl tosylate, 57346-52-8; cyclohexylmethyl *N,N*-dimethylsulfamate, 57346-53-9.

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Reaction of Substituted Benzodioxoles with Methylmagnesium Iodide under Heterogeneous Conditions

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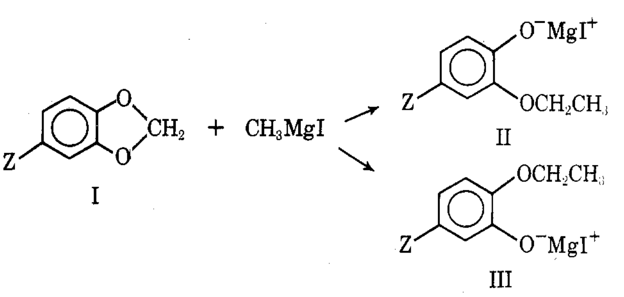
Grignard reagents, when complexed and dissolved by the common ethers, are often unreactive toward C–O single bonds.[2] A typical case is the reaction of 1,3-benzodioxoles with methylmagnesium iodide, which had to be carried out under heterogeneous conditions, between the substrate dissolved in an aromatic hydrocarbon and the insoluble organomagnesium compound.[3]

Reinvestigating such reaction, it has now been found that it proceeds as follows.



a, Z = CH_3
b, Z = H
c, Z = Cl

A partial report has been given.[4]

Results

Stoichiometry. By cleavage of one or the other of the two O–CH_2 bonds, different products, i.e., II and III, are obtained when Z is not hydrogen.

According to a previous report[3] Ia and Ic give only IIa and IIc, respectively. This claim was based on GLC analysis of the corresponding phenols in the hydrolyzed product. Both couples of possible phenolic products IIa–IIIa and IIc–IIIc have been now prepared and it has been shown that in the conditions of the GLC analysis (see Experimental Section) the isomers cannot be resolved. Therefore the reaction products, after hydrolysis and extraction of the phenolic fraction, were analyzed by NMR spectroscopy. Methylethoxyphenols exhibit slightly different CH_2 quartets and CH_3 triplets (at higher fields by 0.02 ppm for IIa); both isomers could be identified and determined in the product mixture from Ia. For the chloroethoxyphenols IIc and IIIc, besides an analogous pattern of the CH_2 and CH_3 signals, an additional difference was found in the peaks of the aromatic protons: an apparent singlet centered at δ 6.70 ppm for IIc and a multiplet with resonance bands centered at 6.77 and 6.59 ppm for IIIc. Both isomers were identified in the product from Ic; their determination was made using the aromatic region of the spectrum.

Ratios x_p = II/(II + III) and $x_m = 1 - x_p$ were evaluated. Results at different conversions and temperatures (from 50 to 68°C) were identical within experimental error. For the reaction of Ia, $x_p \simeq 0.58$ and $x_m \simeq 0.42$, while for the case of Ic, $x_p \simeq 0.25$ and $x_m \simeq 0.75$ were found.

Ethers I and the Grignard reagent were consumed in a 1:1 molar ratio. However, a twofold excess of CH_3MgI was required in order to complete the reaction with good yields of phenols. The formation of a stoichiometric compound between I and the Grignard reagent was not detected. In fact, the solution, separated from the solid phase after a short reaction time, contained the theoretical amount of I and did not evolve gas by water treatment. On the contrary, when phenetole was added to the solution, in the presence of excess CH_3MgI, some of the latter was carried over into the solution. Product IIb bound CH_3MgI in an approximate 1:1 ratio.

Usually, the reactions were carried out on 6 mmol of I in 20 ml of toluene and 18 mmol of CH_3MgI. The latter was partially coordinated to diethyl ether (about 0.1 mol of

Et_2O/mol CH_3MgI) since it was obtained from an ethereal solution by applying heat, reduced pressure, and repeated toluene additions in order to strip out the ether.

The reaction was also carried out on Ib in the presence of $FeCl_3$. For Ib, CH_3MgI, and $FeCl_3$, initially present as 6, 24 and 6 mmol, respectively, the reaction proceeded at about the same rate as the standard reaction (without $FeCl_3$) at the same temperature. In blank experiments, $FeCl_3$ slowly decomposed CH_3MgI with formation of methane and ethane.

Discussion

The structure of solid Grignard reagents has been investigated by x rays in the case of C_2H_5MgBr and C_6H_5MgBr, both crystalline when solvated by two diethyl ether molecules.[5] The same authors reported, in the case of C_6H_5MgBr,[5a] that at high temperature and low pressure the ether content can be lowered, obtaining amorphous polymer forms. The present results on the partial desolvation of CH_3MgI are in agreement with that report.

The presence in the solid reactant, viewed as a polymer, of unsolvated CH_3MgI units justifies its reactivity toward 1,3-benzodioxoles.

Product distribution ratios independent of conversion agree with a scheme of two parallel reactions, involving the oxygen atom para or meta to the substituent. A chloro substituent favors meta attack relative to para. The latter is slightly favored by a methyl substituent. Moreover, an approximate evaluation of reaction rates has shown that Ic is about half as reactive as Ia and Ib, which have nearly the same reactivity. Therefore, the prevailing character of this process can be identified as mildly electrophilic. The attack of magnesium (as a surface atom of the solid Grignard reagent) on one of the oxygen atoms of the substrate (from the solution) is probably involved.

The possibility that the reaction had radical character has been considered. To this purpose, the action of $FeCl_3$ has been tested, since this and similar halides are able to cleave Grignard reagents at low temperature to produce free radicals.[2a] The production of methyl radicals did not enhance the reaction rate enough to suggest a free-radical mechanism.

Experimental Section

Materials. Methylmagnesium iodide was prepared from commercial methyl iodide and magnesium turnings in diethyl ether. The reagent was titrated by acidimetric and gas-volumetric methods.[6] The two methods gave coincident results provided that 1 mol of CH_3MgI was taken to correspond to two acid equivalents (complete oxidation of HI to I_2).

Toluene was reagent grade and was kept over sodium. Sublimed anhydrous ferric chloride was employed.

5-Substituted 1,3-benzodioxoles (Ia–c) were prepared as described.[7,8] 4-Substituted 2-ethoxyphenols (IIa–c) were obtained as reported;[3] the melting point of 4-chloro-2-ethoxyphenol was found to be 57°C.[9] 5-Methyl-2-ethoxyphenol (IIIa) was prepared as described.[3]

5-Chloro-2-ethoxyphenol (IIIc). Concentrated HCl (100 ml) was carefully dropped, during ca. 30 min, into a stirred suspension of granular tin (45 g) in an ethanolic solution (80 ml) of 2-ethoxy-5-nitrophenol (40.3 g).[10] Several hours later, the tin was precipitated as sulfide; from the filtered solution, 5-amino-2-ethoxyphenol hydrochloride was obtained by evaporation. The last step was carried by diazotization and Sandmeyer reaction in the presence of Cu_2Cl_2, followed by steam distillation, extraction by diethyl ether, drying of the ether layer, and removal of the solvent. The product was purified by column chromatography on silica gel (170–230 mesh), eluting with petroleum ether (bp 40–60°C). A liquid was obtained, pure by GLC, bp 282–284°C (760 mm), $n^{27}{}_D$ 1.5480 (yield 5%). Anal. Calcd for $C_8H_9ClO_2$: C, 55.66; H, 5.26; H, 5.26; Cl, 20.54. Found: C, 55.5; H, 5.3; Cl, 20.6. NMR spectrum: CH_3, δ 1.30 (t, 3 H); CH_2, 3.92 (q, 2 H); OH, 5.65 (s, 1 H); H aromatic 6.5–6.8 (m, 3 H).

In an attempt to isolate the undescribed 5-amino-2-ethoxyphenol only tar was obtained.

Reaction Conditions. A Pyrex glass cylindrical vessel (40 cm^3) was equipped with a thermostatted jacket, an outlet on the bottom, reflux condenser, thermometer, nitrogen inlet tube, and connection to rotary pump, besides a helicoidal stirrer, which was usually operated at 850 rpm.

Partial desolvation of the Grignard reagent was obtained by heating the ethereal solution (12–15 cm^3) up to about 90°C under stirring in the reaction vessel, applying a reduced pressure (5–10 Torr) and adding toluene (15–20 cm^3) under nitrogen. This stripping operation was repeated at least four times under continued stirring. A thick paste was finally obtained; the residual diethyl ether was determined by total decomposition of the organomagnesium compound, suspended in toluene, by a slight excess of $FeCl_3$ at 20°C, followed by GLC analysis. One mole of CH_3MgI was found to correspond to 0.67, 0.31, 0.25, 0.10, and 0.10 mol of Et_2O after successive stripping operations (from one to five, respectively).

For reaction, the 1,3-benzodioxolic derivative and toluene were added, usually thermostatting at a temperature in the range 50–70°C. After a time ranging from 2 min to 6 hr (conversion from 5 to 80%) the whole content of the vessel was discharged into ice–water, the mixture was made acidic by 10% aqueous H_2SO_4, the organic layer separated, and the aqueous layer extracted three times by diethyl ether. The combined organic layers were either analyzed by GLC in order to evaluate the conversion, or treated by alkaline extraction in order to isolate the phenolic product for NMR analysis.

Reaction Products. GLC analysis of hydrolyzed reaction products showed the following average yields: IIa + IIIa, 91%; IIb, 88%; IIc + IIIc, 68% of the theoretical.

The unhydrolyzed product from a reaction of Ib at 68°C in standard conditions was separated from the unreacted Grignard reagent, since the former was in the form of light flakes suspended in toluene and the latter in the form of thick paste. Such reaction product was examined by water decomposition and parallel gas-volumetric and GLC analyses; methane and 2-ethoxyphenol (IIb) were found in the molar ratio 1.08:1.

GLC Analysis. Quantitative analyses were performed on a preparative Perkin-Elmer F-21 flame-ionization chromatograph, fit for analytical GLC. The column (2 m i.d. 2 mm) contained 10% SE-301 and 5% neopentyl glycol adipate on Chromosorb P (30–60 mesh). Nitrogen (16 cm^3 min^{-1}) was used as carrier. Temperature was programmed from 50 to 150–170°C (heating rate 9°C min^{-1}). Cumene was used as internal standard and correction factors were determined for all substances.

NMR Measurements. The ^1H NMR spectra were recorded on a Varian HA-100 spectrometer operating at room temperature. Resonance shift values are reported in parts per million relative to hexamethyldisiloxane as internal reference. All samples were 0.1–0.2 *M* CCl_4 solutions.

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Registry No.—Ia, 7145-99-5; Ib, 274-09-9; Ic, 7228-38-8; IIIc, 57428-47-4; methylmagnesium iodide, 917-64-6; 2-ethoxy-5-nitrophenol, 7260-32-4.

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