105° for five hours. The reaction products were separated in the usual manner and distilled fractionally under high vacuum (0.2 mm.). The results are given in Table III.

TABLE III

ANALYSIS OF METHANOLYSIS PRODUCTS FROM THE ETHER-INSOLUBLE RESIDUE AFTER METHYLATION

Fraction	Temp., °C.	Yield, g.	MeO	"Tetra"	"Tri"	"Di"
1	80– 90	3.50	61.5	3.50		
2	90–105	1.25	52.9	0.05	1.20	
3	105–115	1.60	46.5		0.94	0.56
4	115–130	1.85	41.9			1.85
Total grams				3.55	2.14	2.41
Molar per cent.				41.5	26.5	31.8

Analysis of Trimethyl-methyl-galactoside Sirup and Identification of the Components.—The combined intermediate fractions (2.85 g.) from the above distillation were dissolved in 25 cc. of N sulfuric acid and heated on a boiling water-bath for twelve hours. The hydrolysis product was separated in the usual manner, extracted with chloroform, and fractionally distilled under high vacuum. The trimethyl-galactose portion, 1.60 g. (Found: MeO, 41.8), was dissolved in 10 cc. of pyridine and treated with 2.1 g. of trityl chloride. After two days at room temperature a small quantity of water was added to dissolve pyridine hydrochloride and the reaction poured into rapidly stirred ice water. Following two days in the ice box and occasional stirring, the flocculent precipitate was removed by filtration, washed with ice water, and dissolved in acetone. After drying and removal of solvent, a sirup was obtained from which triphenylcarbinol crystallized slowly in the presence of acetone. The non-crystallizable residue, Fraction I, (2.09 g.) comprising triphenylcarbinol and the tritylated galactose derivative, upon treatment with aniline (0.75 g.) in the usual manner gave the anilide of 2,3,4-trimethyl-6-trityl galactose after removal of solvent; m. p. 152°, recrystallized from ethyl alcohol. By calculation on the basis of yield and methoxyl content the 2,3,4-trimethyl-galactose equivalent of Fraction I was determined.

The filtrate from the tritylation reaction was neutralized with silver carbonate and filtered. Silver ion was removed as sulfide and the filtered solution, after treatment with norite, evaporated to dryness. The sirup was taken up in chloroform, filtered, and excess solvent evaporated yielding Fraction II (0.45 g.). Upon treatment with aniline in the usual manner Fraction II gave the crystalline anilide of 2,4,6-trimethyl-galactose; m. p. 178°, recrystallized from ether–ethanol.

The results of the separation are given in Table IV.

TABLE IV

ANALYSIS OF TRIMETHYL-METHYL-GALACTOSIDE SIRUP

Fraction	Yield	MeO	2,3,4-Trimethyl-galactose, g.	2,4,6-Trimethyl-galactose, g.
I	2.90	15.6	1.08	
II	0.45	41.8		0.45
Per cent.			70.6	29.4

Summary

1. Partial hydrolysis of arabo-galactan methyl ether yields a variety of fission fragments including 2,3,5-trimethyl-methyl-l-arabinoside, octamethyl- and heptamethyl-6-d-galactosidogalactose, and a residue comprising mainly 2,4-dimethyl galactose anhydride units.

2. The individual dimethylated residues are shown to be united with each other through the first position, through the first and third positions, through the first and sixth positions, and through the first, third, and sixth positions, respectively.

3. The proportion of 2,4-dimethyl galactose anhydride linked through the first and sixth positions is considerably in excess of that joined at the first and third positions.

4. A tentative structure is presented to represent the repeating unit of arabo-galactan.

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Attempted Asymmetric Syntheses Involving the Grignard Reagent in Optically Active Solvents

BY D. S. TARBELL AND MARK C. PAULSON

In a recent article, it was reported[1] that the Grignard reaction between methylmagnesium iodide and benzaldehyde in dimethylbornylamine as solvent gave optically active methylphenylcarbinol. The same result was obtained using phenylmagnesium bromide and acetaldehyde. This reaction interested us as an example of a new type of asymmetric synthesis,[2] and it suggested

the possibility of obtaining optically active secondary and tertiary alcohols by a synthetic method. We have been unable, however, to obtain optically active carbinols by this reaction under a variety of conditions, using dimethylbornylamine, d-methyl s-butyl ether, or methyl menthyl ether as solvent for the Grignard reagent.

Attempts to duplicate the preparation of methylmagnesium iodide using dimethylbornylamine as a solvent, as reported by Betti and Lucchi,[1] failed. In all cases the quaternary am-

(1) Betti and Lucchi, *Boll. sci. facoltà chim. ind. Bologna*, No. 1-2, 2 (1940) (*C. A.*, **34**, 2354 (1940)).

(2) *Cf.* Ritchie, "Asymmetric Synthesis and Asymmetric Induction," Oxford University Press, London, 1933.

monium salt precipitated almost immediately and the magnesium remained unattacked even after days of standing in the reaction mixture.[3] When methylmagnesium iodide was prepared in ethyl ether, the displaceable ether removed by heating with benzene, and dimethylbornylamine and benzaldehyde added, a poor yield of inactive methylphenylcarbinol was produced. A similar run, (one-tenth mole) in which benzene was omitted and the ether was removed by a water pump, yielded 4 g. of inactive carbinol and 1.4 g. of a heavy straw-colored oil, b. p. 200–210° (20 mm.), m. p. 60–62° after solidification. The oil gave an observed reading of +0.75° at 25° in a polarimeter (0.44 g. diluted to 10 cc. with ethyl alcohol, 1-dm. tube). Later experiments revealed oxidation and reduction occurring in Grignard runs in the absence of ether and led to the identification of this substance as benzalacetophenone, which was doubtless formed by condensation of acetophenone (from the oxidation of methylphenylcarbinol) and benzaldehyde. The rotation of the benzalacetophenone is undoubtedly due to the by-product described in the following paragraph.

In some runs, the methylphenylcarbinol obtained showed a slight positive rotation. That this was due to an optically active by-product from the dimethylbornylamine was shown by blank runs carried out as before, except that the benzaldehyde was omitted; a neutral substance, an amorphous, soft, white solid with a marked terpene-like odor, m. p. ca. 110–120°, was isolated. The small quantity obtained from a one-tenth molar blank run produced a reading of +2.39° (diluted to 10 cc. with ether, 1-dm. tube). The amount isolated was so small that identification was not attempted.

Phenylmagnesium bromide was successfully prepared by heating a flask containing magnesium turnings, dimethylbornylamine and bromobenzene in an oil-bath at 130–140° for four hours, as described by Betti and Lucchi.[1] This was treated with paraldehyde and heated to 110–120° for one hour; fair yields of methylphenylcarbinol (45–60%) were obtained. Optical activity was not consistently produced; in some runs a positive rotation (as high as +0.26°, 4 g. dil. to 10 cc. with 50–50 alcohol–benzene, 1-dm. tube), in others, no rotation was observed. Since careful purification

of the product appeared to eliminate the activity, it is believed that the by-product above caused the rotation.

A much more straight-forward reaction was obtained when d-methyl s-butyl ether (which does not seem to have been reported in the active form previously) was used as the solvent for the Grignard reaction. Completely inactive methylphenylcarbinol was obtained in 60–68% yield, using either methylmagnesium iodide or phenylmagnesium bromide with the proper aldehyde. The product in each case was checked by preparation of the 3,5-dinitrobenzoate, m. p. 90°, and mixed melting point of this derivative with that of an authentic sample.

It seemed desirable to try another optically active ether with a higher rotation than the s-butyl ether, and methyl menthyl ether, $[\alpha]^{25}$D −95.6°, was prepared and studied. In this connection, it is interesting to note that Wegler and Ruber[4] found that in the preferential esterification of d,l-methylphenylcarbinol by acetic anhydride in the presence of optically active bases, the activity of the ester mixture varied greatly with the base used.

Methyl menthyl ether proved to be an unsuitable solvent for the Grignard reaction. When magnesium was treated with methyl or ethyl iodide in this ether, the magnesium quickly became coated with an insoluble white material which prevented further reaction. The coating formed by ethyl iodide gave a positive Gilman Grignard color test with Michler ketone. The Grignard reagents were better prepared in diethyl ether, which was then removed in vacuo in a nitrogen atmosphere with a capillary to prevent bumping. When most of the ether had been removed, methyl menthyl ether was added (75 to 100 cc. for tenth-molar runs) and the vacuum (water pump) again applied for several hours. Usually after the first half-hour, the entire contents of the flask solidified to a white solid. This was probably the Grignard etherate involving the optically active ether. Methylmagnesium iodide prepared in this manner reacted with n-butyraldehyde to produce, instead of the expected s-amyl alcohol, n-butyl alcohol and methyl n-propyl ketone. The alcohol was identified by preparation of its 3,5-dinitrobenzoate and a mixed melting point with the corresponding derivative of an authentic sample; the ketone in like fashion through its

(3) This agrees with the observations of Stadnikoff and Weizmann, J. prakt. Chem., 112, 177 (1926), who attempted to prepare Grignard reagents in dimethylaniline solution.

(4) Wegler and Ruber, Ber., 68, 1055 (1935).

2,4-dinitrophenylhydrazone. The *n*-butyraldehyde is evidently reduced by the magnesium halide alkoxide of *s*-amyl alcohol which is formed by primary addition of the Grignard.

The failure to get an asymmetric synthesis in the reaction with *d*-methyl *s*-butyl ether, at least, is rather surprising. A possible explanation is that the organomagnesium compound is coordinated with two molecules of the ether in such a way that the complex has a plane of symmetry.[5]

Preparation of Materials

Bornylamine (a mixture of the diastereoisomers, bornylamine and neobornylamine, hereafter referred to as the former) was prepared from *d*-camphor in 83% yield (crude) using Ingersoll's modification[6] of the Leuckart method. The crude product was used in the preparation of dimethylbornylamine, since the latter product is much easier to purify.

Dimethylbornylamine was prepared by adding dimethyl sulfate to a vigorously stirred mixture of the crude bornylamine, aqueous sodium hydroxide and benzene. A Schotten–Baumann reaction employing benzoyl chloride effectively separated the mixture of secondary and tertiary amines; the organic material was isolated in ether and the tertiary amine extracted from the benzamide by dilute hydrochloric acid; yield 44.5% (purified amine); b. p. 92° (13 mm.). *Rotation.* α −1.01° (0.525 g. dil. to 25 cc. with dry benzene, 1-dm. tube), $[\alpha]^{24}$D −48.1°. No gas was evolved when this product was treated with methylmagnesium iodide.

Hydrolysis of the N-methyl-N-bornylbenzamide proved too difficult to make the recovery of the secondary amine practicable.

Optically Active Methyl *s*-Butyl Ether.—*s*-Butyl alcohol was partially resolved by the method of Pickard and Kenyon,[7] using the modification of Sprung and Wallis and of Viditz.[8] The ether[9] was prepared by the Williamson syn-

(5) *Cf.* Whitmore and George, abstracts of papers presented at Atlantic City, September, 1941.

(6) Ingersoll, Browns, Beauchamp and Jennings, This Journal, **58**, 1808 (1936); Leuckart and Bach, *Ber.*, **20**, 104 (1887).

(7) Pickard and Kenyon, *J. Chem. Soc.*, **99**, 45 (1911); **103**, 1923 (1913).

(8) Sprung and Wallis, This Journal, **56**, 1715 (1934); Viditz, *Biochem. Z.*, **259**, 294 (1933).

(9) This compound was prepared in the inactive form by Bennett, *J. Chem. Soc.*, 1930 (1928).

thesis, treating the alkoxide (prepared from 42 g. of *s*-butyl alcohol and 8 g. of sodium) with 52 g. of methyl iodide; yield, 83%, b. p. 59–60°, alcohol of rotation αD +7.5° (homogeneous, 1-dm. tube) produced an ether of αD +12.19° (homogeneous, 1-dm. tube).

Methyl Menthyl Ether.—Sodium (24 g.) was added in approximately 1-g. portions to 172 g. of *l*-menthol dissolved in 175 cc. of dry toluene. The mixture was heated on a steam-bath for twenty-seven hours. At the end of this time, 4.1 g. of unreacted sodium was removed from the flask. The solution was cooled and 128 g. of methyl iodide was added dropwise. After the initial reaction had subsided the flask was warmed in an oil-bath at 75° for four hours. Most of the toluene was then removed under diminished pressure; the residue of sodium iodide was filtered off and was washed with ether to remove any reaction product. The product was fractionated twice under diminished pressure. Thirty-seven grams of menthol was recovered from the first fractionation. The second fractionation was carried out in the presence of a few small pieces of sodium to aid in removal of traces of menthol; yield, 109.5 g. (74%); b. p. 83° (12 mm.); b. p. 197° (uncor. 736.5 mm.); n^{23}D 1.4427; $[\alpha]^{25}$D −95.6°; $d^{25}{}_{25}$ 0.8584; homogeneous rotation, −82.06°, 1-dm. tube. *Anal.*[10] Calcd. for $C_{11}H_{22}O$: C, 77.56; H, 13.03. Found: C, 77.56; H, 12.91.

Summary

1. Methylphenylcarbinol prepared by the Grignard reaction in optically active methyl *s*-butyl ether is optically inactive. The carbinol prepared in dimethylbornylamine is also inactive, although a neutral optically active impurity is formed in the reaction.

2. Methyl menthyl ether is not a suitable solvent for the Grignard reaction; *n*-butyl alcohol and methyl *n*-propyl ketone were obtained when methylmagnesium iodide was treated with *n*-butyraldehyde.

(10) Analysis by R. W. King. Tschugaeff, *J. Russ. Phys.-Chem. Ges.*, **34**, 606 (1902); *Chem. Zentr.*, **73**, II, 1238 (1902), reported $d^{20}{}_4$ 0.8607 and $[\alpha]$D −95.67°, but gave no other constants.