reaction with sodamide was complete, 7.0 g. of *o*-methylbenzyl chloride[3] was added dropwise. This reaction mixture was boiled under reflux for two hours, cooled, and washed several times with water. After removal of the toluene *in vacuo*, the residual oil was distilled yielding 7.1 g. (60%) of a colorless oil; b. p. 116–117° at 1.2 mm.; $n^{21}D$ 1.4984.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.15; H, 8.65. Found: C, 71.25; H, 8.74.

Hydrolysis of a sample of 2,2-dimethyl-4-(*o*-methylbenzyloxymethyl)-1,3-dioxolane (2.0 g.) was accomplished by boiling it for one hour with a solution containing 14 ml. of alcohol, 5 ml. of water and 0.2 ml. of concentrated sulfuric acid. The mixture was neutralized with sodium carbonate, and the organic layer was separated and distilled. There was obtained 0.75 g. (45%) of a colorless oil; b. p. 149–151° at 0.4 mm.; $n^{21}D$ 1.5330.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.52; H, 8.11.

Attempts to prepare 3-(*o*-methylbenzyloxy)-1,2-propanediol by the reaction of the sodium salt of *o*-methylbenzyl alcohol with epichlorohydrin or glycerol α-monochlorohydrin were unsuccessful.

Since 3-(*o*-methylbenzyloxy)-1,2-propanediol is an analog of myanesin (3-(*o*-toloxy)-1,2-propanediol), it was tested for physiological action by intraperitoneal injection into mice.[4] It was found that even at lethal dosages muscular paralysis was incomplete.

(3) Newman, THIS JOURNAL, **62**, 2295 (1940).

(4) Physiological tests were made by F. M. Berger, M.D., Department of Pediatrics, University of Rochester School of Medicine, Rochester, New York.

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Five New Tertiary Carbinols and Four New Aliphatic Hydrocarbons

In the course of work on the mechanism of anomalous Grignard reactions,[1] five tertiary carbinols were obtained, which are believed to be new. Four of these were converted to the corresponding hydrocarbons.

Compound	B. p.[a] °C.	Mm.	$n^{20}D$	Yield, %	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
2,4,5-Trimethylheptan-4-ol[b]	54–55	3	1.4382	15	$C_{10}H_{22}O$	75.9	76.3	13.9	13.9
3,4-Dimethyloctan-4-ol[c]	64–65	3	1.4418	20	$C_{10}H_{22}O$	75.9	75.8	13.9	14.0
3,4-Dimethylnonan-4-ol[d]	68–69	2	1.4430	15	$C_{11}H_{24}O$	76.7	76.2	13.9	14.1
2,6-Dimethyl-4-isopropylheptan-4-ol[e]	48–49	1	1.4448	20	$C_{12}H_{26}O$	77.4	77.6	14.0	13.9
2,6-Dimethyl-4-isobutylheptan-4-ol[f]	72–73	2	1.4390	15	$C_{13}H_{28}O$	78.0	77.6	14.0	13.9
2,4,5-Trimethylheptane[g]	49.5	18	1.4160		$C_{10}H_{22}$	84.5	84.6	15.5	15.1
3,4-Dimethyloctane[g]	58.0–58.4	20	1.4182		$C_{10}H_{22}$	84.5	84.6	15.5	15.0
3,4-Dimethylnonane[g]	75.0–75.2	18	1.4223		$C_{11}H_{24}$	84.8	84.9	15.2	14.8
2,6-Dimethyl-4-isobutylheptane	81.9–82.5	20	1.4238		$C_{13}H_{28}$	84.6	84.3	15.4	15.0

[a] Uncorrected. By the interaction of *s*-BuMgBr and MeCOBu-*i*. [c] By the interaction of *s*-BuMgBr and MeCOBu-*n*. [d] By the interaction of *s*-BuMgBr and MeCOAm-*n*. [e] By the interaction of *i*-PrMgBr and *i*-BuCOBu-*i*. [f] By the interaction of *i*-BuMgBr and *i*-BuCOBu-*i*. Skraup and Freundlich, *Ber.*, **55**, 1080 (1922), report that they made this by the action of *i*-BuMgBr on isovaleric ester, but say that the pure carbinol could not be obtained, since it decomposed when distilling in a high vacuum. No physical constants were given. [g] Calculations of the physical constants of this are given by Francis, *Ind. Eng. Chem.*, **35**, 442–448 (1943).

In the conversion of the carbinols to the hydrocarbons, the former were dehydrated to the olefins with naphthalene-2-sulfonic acid, and the olefins were fractionated, the column used being packed to a length of 12 inches with Fenske helices, and fitted with a total-reflux-variable-take-off still head. They were then reduced in glacial acetic acid with Adams catalyst and hydrogen at 50 p. s. i. pressure until no unsaturation could be detected with a solution of bromine in carbon tetrachloride. The hydrocarbons were fractionated through the column described above.

(1) Shine and Turner, "The Anomalous Reactions of Grignard Reagents (I)," submitted for publication in THIS JOURNAL.

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RECEIVED NOVEMBER 5, 1948

COMMUNICATIONS TO THE EDITOR

EXCHANGE REACTIONS BETWEEN CERIUM(III) AND CERIUM(IV) AND BETWEEN IRON(II) AND IRON(III)

Sir:

We have studied the exchange reaction between cerium(III) and cerium(IV) in perchloric acid and in sulfuric acid solutions. Using electrical migration methods to partially separate the reactants we have found no evidence that the exchange is measurably slow. The 30-day Ce^{141} used as cerium(III) tracer was obtained from the Clinton Laboratories on allocation from the U. S. Atomic Energy Commission. It was purified by precipitation of cerium(III) fluoride and ammonium hexanitratocerate(IV). The Ce^{141} content of solutions was determined by gamma-counting. Cerium was determined by titration with iron(II) sulfate. In sulfuric acid solutions cerium(IV) migrated toward the anode, cerium(III) toward the cathode. In perchloric acid solutions both ions migrated toward the cathode, cerium(III) being the more mobile. Samples enriched in each

ion were collected. The enrichment factors (R/R_0)[1] achieved were 1.5 to 50 and <0.01 for sulfuric acid solutions and 1.2 to 1.4 and 0.6 to 0.9 for perchloric acid solutions. Three runs were made in 1.0 f. sulfuric acid (0.02 f. cerium, $R_0 = 0.65$ to 1.75, *ca.* 15°), and nine runs in perchloric acid (0.1 f. cerium, $R_0 = 1.1$ to 1.6, 4°), five of these in 1.0 f. acid and four in 1.8 f. acid and in the dark. Within the estimated accuracy of the experiments (5 to 20%, depending on the enrichment achieved) complete exchange occurred in all runs during the separation time (45 to 90 minutes for sulfuric acid solutions, 2.5 to 4 hours for perchloric acid solutions).

We have also studied the exchange reaction between iron(II) and iron(III) in perchloric acid solutions and, using the sintered glass disk diffusion method of separation,[2] have found no evidence that the exchange is measurably slow (18.5-day half-time) as reported by Van Alten and Rice.[2] The 47-day Fe^{59} used as iron(III) tracer was prepared by the Co^{59} (n,p) reaction in the Washington University cyclotron. It was purified by extraction of iron(III) chloride into isopropyl ether. Thin (*ca.* 0.5 mg./cm.) solid samples were beta-counted. Iron was determined by titration with cerium(IV) sulfate. We found the diffusate enriched ($R/R_0 = 0.6$ to 0.8) in iron(II); Van Alten and Rice[2] reported enrichment of the diffusate in iron(III). Two runs were made in 1.0 f. perchloric acid (0.1 f. iron, $R_0 = 0.3$, *ca.* 25°) and two under Van Alten and Rice's conditions, 3.0 f. perchloric acid, 0.02 f. iron, $R_0 = 0.24$, *ca.* 25°. One of the latter runs was performed in the dark. Within the estimated 10% accuracy of the experiments, complete exchange occurred in all runs during the one to two-hour diffusion time.

It is of course possible that the exchange reactions were catalyzed. Chloride, nitrate and sulfate were not detected as impurities in the components of the reaction mixtures. However, undetectable amounts of these or other impurities might have been effective catalysts. Heterogeneous catalysis is also a possibility, especially for the iron exchange reaction, since the diffusing reactants were exposed to a large glass surface during the separation.

(1) R = Ce(IV)/Ce(III) or Fe(III)/Fe(II) in the enriched fraction. R_0 is the same ratio in the original solution.

(2) Van Alten and Rice, THIS JOURNAL, **70**, 883 (1948).

DEPARTMENT OF CHEMISTRY
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RECEIVED MARCH 31, 1949

STREPTOMYCES ANTIBIOTICS. XXIII. ISOLATION OF NEOMYCIN A

Sir:

Crystalline neomycin A sulfonic acid salts have been obtained which on regeneration yield neomycin A hydrochloride.

Neomycin was discovered by Waksman and Lechevalier.[1] It is a new antibiotic elaborated by *Streptomyces fradiae* which is active against streptomycin-resistant bacteria, including tuberculosis organisms. The initial adsorption of the antibiotic from the culture medium and its elution has been reported.[1] A search was conducted for a method of preparing a pure salt of neomycin. During this time, evidence has been obtained that the neomycin activity is due to more than one chemical entity; hence, one may define it as a "neomycin-complex."[2] The substance isolated, as described herein, has been designated neomycin A.

Countercurrent distribution of concentrates (*ca.* 100 units/mg.) with a water–butanol–toluenesulfonic acid system gave purified fractions showing 500–700 units/mg. For larger scale work, the same degree of purification was achieved by picric acid precipitation, conversion of the picrate to the hydrochloride, and chromatography over alumina using aqueous methanol.

Treatment of concentrates (500–700 units/mg.) with sodium *p*-(*p'*-hydroxyphenylazo)-benzenesulfonate, methyl orange and orange II yielded the corresponding crystalline sulfonic acid salts. The first-mentioned salt was prepared in 20% aqueous methanol. Five recrystallizations of the product from the same solvent yielded crystalline material apparently having constant properties for the last three crystallizations. The ultraviolet absorption spectrum of a *p*H 8 phosphate buffer ($M/20$) solution shows a prominent band at 3700Å. ($E^{1\%}_{1\,cm.}$ 410). Heated on the microblock, the salt decomposes at about 225° and does not melt up to 300°. Mr. John Lally and Dr. H. B. Woodruff found that this salt showed about 650 neomycin units/mg. with *B. subtilis* as test organism.

Regeneration of the recrystallized neomycin A *p*-(*p'*-hydroxyphenylazo)-benzenesulfonate with aqueous hydrochloric acid and butanol and subsequent addition of acetone to the aqueous solution caused precipitation of neomycin A hydrochloride as a white amorphous powder, $[\alpha]^{25}D$ +83° (*c*, 1.0 in water). The activity was about 1700 neomycin units/mg.; activity was also shown against tubercle bacilli *in vitro*. In the ultraviolet, only end absorption was observed. On the microblock, it began to darken at about 220° and melted with decomposition at 250–260°. Conversion of a portion of this sample of neomycin A back to the *p*-(*p'*-hydroxyphenylazo)-benzenesulfonate gave material which after two recrystallizations still showed the same properties described above.

Countercurrent distribution of regenerated neomycin A hydrochloride in a system composed of aqueous *p*-toluenesulfonic acid and *n*-butanol[3]

(1) Waksman and Lechevalier, *Science*, **109**, 305 (1949).

(2) Personal communication: Swart, Hutchison and Waksman, in press.

(3) Titus and Fried, *J. Biol Chem.*, **168**, 393 (1947).