of δ-hydroxyvaleric acid to the lactone is not complete but that 8% acid is present in the final equilibrium mixture.

Action of Sodium Acetate on Products of Direct Chlorination.—Fifty-five grams of the monochlorinated methyl ester fraction from the chlorination of hexoyl chloride was digested in 70 g. of acetic acid with 45 g. of sodium acetate for thirty hours. Upon treatment as previously described, 55 g. of oil was obtained. Care was taken to extract all the products of the reaction from the aqueous wash-waters.

The material thus obtained was thoroughly saponified with an excess of 50% aqueous alcoholic potassium hydroxide solution. Sulfuric acid was added and the reaction products were extracted with ether. At least twenty extractions were necessary but the recovery was almost quantitative; b. p. (5 mm.) 98–105°.

The mixture of acids and lactones thus obtained had the following characteristics

Iodine value (bromine absorption)	51
Saponification equiv.	110
Sapn. value (Koettstorfer)	508
Neutralization equiv.	231
Neut. value	242
Calcd. for $C_6H_{10}O_2$ { iod. value	222
Calcd. for $C_6H_{10}O_2$ { sapn. equiv.	114
Calcd. for $C_6H_{12}O_3$ { neut. equiv.	132
Calcd. for $C_6H_{12}O_3$ { neut. value	424

The above iodine values indicate that there is 23% of unsaturated acid present. This is an approximate estimate of the amount of β-chloro ester originally present. The difference between the saponification and neutralization values is a measure of the lactones. This corresponds to 52% γ- and Δ-chloro esters, approximately.

In order to verify these deductions the reaction mixture was caused to react in methanol solution with hydrogen chloride. It was found that the product contained 15.8% chlorine which agrees with the calculated value of 16.2%. The higher proportion of beta, gamma and delta isomers shown to be present makes it reasonable to assume that the remaining 25% is largely α-chloro ester. Proof of this assumption, however, could not be obtained by any of the several methods tried.

The chlorinated esters of hexoic acid, octoic and octadecoic acids were subjected to this reaction with comparable results in each case.

Summary

Several new chlorinated acids were prepared and their reaction with sodium acetate in acetic acid studied. It was thus found that characteristic reaction products, depending on the position of the chlorine, were formed.

These data were used to estimate the proportion of monochlorinated isomers formed in the direct chlorination of representative long-chain methyl esters. It is thus shown that approximately half of the chlorine is in the gamma or delta position and 25% is in the beta position.

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[CONTRIBUTION FROM RIDBO LABORATORIES, INC.]

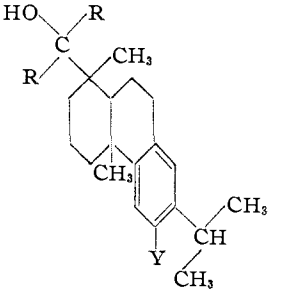
Studies on Resin Acids. I. Carbinols

BY HAROLD H. ZEISS

The work of Fieser, Campbell and Morgana[1,2] on reactions of the resin acids has stimulated interest in this group of natural products. The major portion of their work has been concerned chiefly with substitution on the aromatic ring of dehydroabietic acid. The preparation of 6-hydroxydehydroabietinol was of particular significance in this work because of its reported estrogenic activity. These studies have been extended in a new direction with the purpose of obtaining other derivatives having perhaps enhanced physiological properties.

The primary carbinols of the resin acids have usually been prepared by reduction methods. This present paper describes the synthesis of tertiary carbinols *via* the Grignard reaction and further confirms the conclusions of Campbell and Todd[3] regarding the configuration of the C_1 carboxyl groups of dehydroabietic and podocarpic acids. According to the excellent paper of those authors the carboxyl group of dehydroabietic acid occupies a *trans* position in space relative to the angular C_{12} methyl group. On this basis Stewart models admit the possibility of a diphenylcarbinol although a very close fit is involved.

Use of the Grignard reaction as employed by Wieland, *et al.*,[4] on the bile acid esters was found to be effective in the preparation of diphenyl-*t*-dehydroabietinol (I) from methyl dehydroabietate. Further application of the method to the



I. R = C_6H_5, Y = H
II. R = C_6H_5, Y = OH

methyl ester of 6-methoxydehydroabietic acid gave after demethylation the corresponding diphenylcarbinol (II). Methyl O-methylpodocarpate in which the carbomethoxy group is *cis* to the C_{12} angular methyl group failed to react detectably under the same conditions with phenylmag-

(1) (a) Fieser and Campbell, THIS JOURNAL, **60**, 159 (1938); (b) **60**, 2631 (1938); (c) **61**, 2528 (1939).

(2) Campbell and Morgana, *ibid.*, **63**, 1838 (1941).

(3) Campbell and Todd, *ibid.*, **64**, 928 (1942).

(4) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, **161**, 80 (1926).

nesium bromide in accord with the experiments of Sherwood and Short.[5] This lack of reactivity is readily explained by the steric hindrance exerted by the angular methyl group.

Experimental[6]

Diphenyl-*t*-dehydroabietinol (I).—A solution of 38 g. of methyl dehydroabietate in 100 ml. of dry ether was added to a refluxing ethereal solution of phenylmagnesium bromide prepared from 7 g. of magnesium turnings and 43 g. of bromobenzene in 200 ml. of dry ether. The mixture was refluxed for two hours, the ether was removed and the viscous residue heated on the steam-bath for two hours. After standing overnight the mass was hydrolyzed with 10% sulfuric acid and ice with stirring under a layer of ordinary ether. Both layers were transferred to a separatory funnel and the acidic layer removed. After washing the ether layer with several portions of 10% sulfuric acid and finally with distilled water to neutrality, solvent ether was removed and the residue was steam distilled to remove diphenyl. The mass was next dried in ether over sodium sulfate and then vacuum distilled, the main fraction of carbinol distilling between 186–191° (8–9 mm.) as a pale yellow oil; yield 33.5 g. (63%).

Anal.[7] Calcd. for $C_{32}H_{38}O$: C, 87.61; H, 8.73. Found: C, 87.22, 87.65; H, 8.54, 8.69.

Diphenyl-*t*-6-hydroxydehydroabietinol (II).—Methyl 6-methoxydehydroabietate (8.6 g.) in 20 ml. of absolute ether was added to an ether solution of phenylmagnesium turnings. The procedure was the same as above. Cleavage of the ether linkage seems to have occurred during hydrolysis with 10% sulfuric acid, after which the crude hydroxy carbinol residue was steam distilled to remove diphenyl and dried in ether. After removal of the ether the residue was crystallized three times from methanol giving 2.8 g. (24.5%) of transparent prisms of diphenyl-*t*-6-hydroxydehydroabietinol; m. p. 194–196°. Repeated recrystallization from glacial acetic acid did not alter the melting point.

Anal.[8] Calcd. for $C_{32}H_{38}O_2$: C, 84.53; H, 8.42. Found: C, 84.70, 84.45; H, 8.85, 8.82.

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Summary

The synthesis of diphenyl-*t*-dehydroabietinol and diphenyl-*t*-6-hydroxydehydroabietinol by the Grignard method has been described. Further proof of the *trans* configuration of the C_1 carboxyl group in dehydroabietic acid through the preparation of these compounds is also given.

(5) Sherwood and Short, *J. Chem. Soc.*, 1006 (1938).

(6) The carbinols reported here are being submitted to pharmacological tests.

(7) Analysis by the author.

(8) Analysis by Mrs. B. G. Zeiss.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Heterocyclic Basic Compounds. X. 4,8-Diaminoquinoline and Derivatives

BY R. W. GOULEY,[1] G. W. MOERSCH[1,2a] AND HARRY S. MOSHER[2b]

Of all the quinoline derivatives which have been tested as antimalarials, only the derivatives of 4-amino- and 8-aminoquinolines have shown any appreciable activity. For this reason it was decided to investigate derivatives of 4,8-diaminoquinoline. Although other diaminoquinoline compounds, particularly derivatives of 4,6-diaminoquinoline, have shown promise in chemotherapy,[3] no reports appear in the literature on the synthesis and properties of 4,8-diaminoquinoline and its derivatives. Considerable difficulty was experienced in this work and it was necessary to abandon several proposed methods of synthesis before a successful route was uncovered.

The synthesis of 4-hydroxy-8-nitroquinoline was first attempted through the ethoxymethylenemalonic ester condensation with *o*-nitroaniline. Although the condensation, cyclization and hydrolysis steps were successful, we were unable to decarboxylate the 3-carboxy-4-hydroxy-8-nitroquinoline. The successful decarboxylation of this substance[4] has since been reported[5] by heating the silver salt of the acid in boiling Dowtherm.

In applying the method of Meisenheimer[6] to various quinoline derivatives, the N-oxide of 5-nitroquinoline (I) was treated with phosphorus oxychloride; 2-chloro-5-nitroquinoline[7] (IV) 35%, 4-chloro-5-nitroquinoline (III) 10%, and 3-chloro-5-nitroquinoline (V) 20% were obtained. The identity of the 2-chloro-5-nitroquinoline was confirmed by its conversion to the known 5-nitrocarbostyril[7]; the structure of the 4-chloro-5-nitroquinoline (III) was proved by demonstrating its identity with one of the products obtained from the nitration of 4-chloroquinoline (II); and the third isomer was assumed to be 3-chloro-5-nitroquinoline (V) by elimination. This assumption has now been verified by comparison of this isomer with an authentic sample[8] whose

(1) Parke, Davis and Company post-doctoral fellow, 1945.

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(3) Jensch, *Angew. Chem.*, **50**, 893–895 (1937)

(4) Riegel, *et al.*, THIS JOURNAL, **68**, 1264–1266 (1946).

(5) Baker, Lappin, Albisetti and Riegel, *ibid.*, **68**, 1267 (1946).

(6) Meisenheimer, *Ber.*, **59**, 1848–1853 (1926); Bachmann and Cooper, *J. Org. Chem.*, **9**, 302–309 (1944).

(7) Claus and Setzer, *J. prakt. Chem.*, (2) **53**, 392–396 (1896); Deinet and Lutz, THIS JOURNAL, **68**, 1325–1426 (1946).

(8) We are greatly indebted to Dr. Riegel of Northwestern University for this sample of 3-chloro-5-nitroquinoline.