in an ice-bath to obtain crystallization. Two recrystallizations usually sufficed to give a product whose melting point did not change upon further recrystallization. Other combinations of solvents found suitable for recrystallization were *n*-butanol–ether and acetone–ether. Table III contains pertinent data on the compounds prepared. Attempts to prepare 4-chloropentyldiethylamine by heating 1,4-dichloropentane, sodium iodide, and diethylamine resulted in the formation of a mixture one of whose main components was the ethochloride of 1-ethyl-2-methylpyrrolidine.

Acknowledgment.—It is a pleasure to acknowledge the generosity of Mr. J. K. Lilly, who defrayed the cost of this investigation.

Summary

The vapor-phase photochemical chlorination of 1-chloropentane was carried out with the isolation by rectification of the 1,3-, 1,4-, and 1,5-dichloropentanes. The 1,1- and 1,2-isomers were not separated from each other.

A new synthesis of chloroalkyldialkylamines has been developed. The method consists of treating a chloroiodoalkane with diethylamine at room temperature. The iodochlorides were prepared by heating the corresponding dichlorides with sodium iodide in anhydrous acetone.

The amines prepared in good yields included: 3-chloropropyldiethylamine, 3-chlorobutyldiethylamine, 3-chloropentyldiethylamine, 4-chloropentyldiethylamine, and 5-chloropentyldiethylamine, all of which were isolated as the hydrochlorides.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Condensation of Diketones with Phenol[1]

BY JOSEPH B. NIEDERL AND RICHARD H. NAGEL[2]

With the extension of the systematic study of the condensation of carbonyl compounds with phenols,[3] it was expected that the various phenomena encountered in monoketone–phenol condensations should be applicable also to the diketone condensations. This expectation was not always realized in the case of the di- and trihydroxyphenols[4] but in the case of phenol itself the expected condensation products were obtained. Thus when the γ-diketone, acetonylacetone, was condensed with phenol in the presence of dry hydrogen chloride in the ratio of 4 moles of phenol to 1 mole of diketone, the predicted double alkylidene-diphenol, 2,2,5,5-tetrakis-(4′-hydroxyphenyl)-hexane (I) was obtained. This tetraphenol was characterized by functional and nuclear substituted derivatives, such as esters [acetate (Ia) and propionate (Ib)], nitro (Ic) and mercury derivatives (Id).

When the α-diketone, benzil, was condensed with phenol, the reaction took a different course. These two compounds had been condensed by Liebig[5] under somewhat drastic conditions by fusing them at 180° in the presence of zinc chloride, yielding the lactone of *o*-hydroxytriphenylacetic acid, melting at 129°. Under the milder conditions of the present experiment, a crystalline compound was obtained, melting at 212° and analyzing for the combination of two moles of phenol and 1 mole of benzil with the loss of 1 mole of water (II). This compound formed a diacetate (IIa) and a dipropionate (IIb). Thus the present condensation product appears to be an entirely different substance and checks perfectly for benzoyl-4,4′-dihydroxy-tritan (II). This compound has been reported previously by Kempinski[6] who obtained it as a not further characterized red powder by fusing α,α-dichloro-α-phenylacetophenone with phenol in the presence of zinc chloride.

It suggests itself that the general reaction mechanism as advanced by McGreal and Niederl[7] for carbonyl compound–phenol condensations might be also applicable to the two types of condensations presented in this paper. In both cases, undoubtedly, also an intermediate "phenolhydrin" type of a compound would form. This

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(1) The contents of this communication were part of a paper entitled "Diketone–Phenol Condensations" delivered before the Organic Division at the Cincinnati meeting of the American Chemical Society in April, 1940.

(2) Abstracted from a portion of the thesis submitted to the faculty of the Graduate School of New York University by Richard H. Nagel in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) J. B. Niederl and co-workers, THIS JOURNAL, **50**, 2230 (1928); **51**, 2426 (1929); **58**, 657 (1936); **59**, 1113 (1937); **61**, 345, 348, 1005, 1785 (1939); **62**, 320, 322, 324, 1157 (1940).

(4) Niederl and Nagel, *ibid.*, **62**, 3070 (1940); **63**, 307, 580 (1941).

(5) Liebig, *Ann.*, **350**, 206 (1908).

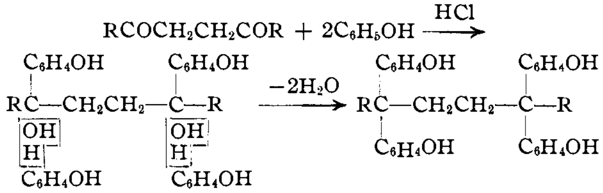
(6) Kempinski, *Bull. soc. chim.*, [3] **7**, 609 (1892).

(7) M. E. McGreal and J. B. Niederl, "Abstract of Papers, 97th Meeting, Am. Chem. Soc." Baltimore, Md., 1939, M. pp. 5–7.

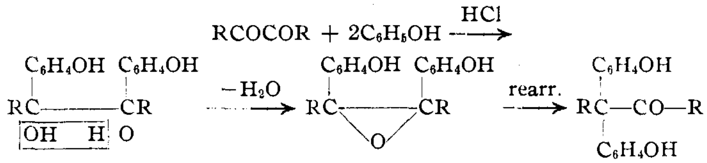
intermediate, then, in the case of the γ-diketone would react with an additional two molecules of phenol to yield by intermolecular dehydration the respective double alkylidene-diphenol essentially as previously postulated[8] and as illustrated in reaction "A."

In the case of the α-diketone, however, pinacol-pinacolone rearrangement seems to precede the otherwise normally occurring additional phenol condensation, as suggested by P. Papadakis,[9] with the formation of a pinacolone type of tertiary aromatic ketone, the above benzoyl-4,4'-dihydroxytritan (II) as shown in reaction "B." This ketone, the carbonyl group of which appears to be rather inert, was therefore reduced to the respective secondary alcohol, the benzhydryl-4,4'-dihydroxy-tritan (III), of which in turn a crystalline tri-acetate (IIIa) was prepared for further structural confirmation.

REACTION "A"



REACTION "B"



Experimental

2,2,5,5-Tetrakis-(4'-hydroxyphenyl)-hexane (I).—Two moles (188 g.) of phenol and one-half mole (57 g.) of acetonylacetone were placed in a one-liter three-necked round-bottomed flask provided with a gas inlet tube. Dry hydrogen chloride gas was passed into the reaction mixture at room temperature for six hours, and then the flask was tightly stoppered to keep the reactants in an atmosphere of the condensing agent, and left standing at room temperature for two weeks, in which time the mixture had completely solidified to a deep-red crystalline mass. The flask was then provided with a reflux condenser, 200 cc. of acetic acid added, and the mixture refluxed for four hours while at intervals small amounts of zinc dust were introduced. At the end of this time the color had lightened considerably. After filtration the residue, containing the tetraphenol, was washed repeatedly with hot water to free it from zinc chloride, then dissolved in boiling 95% ethyl alcohol and filtered into an evaporating dish. Upon cooling, fine white crystals with a pink tinge were obtained. After two further recrystallizations from the same solvent, a completely white product resulted. The crystals are soluble in Claisen solution, m. p. 298° (uncor.).

Anal. Calcd. for $C_{30}H_{30}O_4$: C, 79.29; H, 6.61. Found: C, 79.76; H, 6.69.

Acetate (Ia).—Ten grams of the condensation product was dissolved in an excess of acetic anhydride (50 cc.) and the mixture was refluxed for six hours. On standing in an evaporating dish the acetate crystallized out; it was recrystallized from alcohol, m. p. 186° (uncor.).

Anal. Calcd. for $C_{38}H_{38}O_8$: C, 73.31; H, 6.11; mol. wt., 622. Found: C, 73.10; H, 6.61; mol. wt., 610.

Propionate (Ib).—A mixture of 2 g. of the above condensation product and 25 cc. of propionic anhydride was refluxed for four hours, then poured into cold water and let stand, with occasional shaking, until the excess solvent had hydrolyzed. The semi-solid was transferred onto a porous tile, then the mass was recrystallized from 95% ethyl alcohol, m. p. 116–118° (uncor.).

Anal. Calcd. for $C_{42}H_{46}O_8$: C, 74.34; H, 6.79. Found: C, 74.24; H, 7.04.

Nitro Derivative (Ic).—One gram of the phenol condensate was warmed on the water-bath with concentrated nitric acid in excess till no more brown fumes were evolved. The undissolved residue was separated from the solution by filtration through a sintered glass funnel, washed repeatedly with water, and recrystallized from alcohol. The crystals decompose at 300–305°. The filtrate was evaporated to dryness on the steam-bath, leaving a residue of picric acid.

Anal. Calcd. for $C_{30}H_{22}O_{20}N_8$: C, 44.22; H, 2.70; N, 13.76. Found: C, 43.87; H, 3.02; N, 13.50.

2,2,5,5 - Tetrakis - (4' - hydroxy - 3',5' - diacetoxymercuryphenyl)-hexane (Id).[10]—Two grams of the tetraphenol was dissolved in 25 cc. of ethyl alcohol, and to the solution 5 cc. of glacial acetic acid was added, and the mixture warmed until the phenol had completely dissolved. To the solution was then added 11.2 g. of mercuric acetate dissolved in 50 cc. of ethyl alcohol containing 1 cc. of acetic acid. The solution was heated on a steam-bath for two hours, when a precipitate began to settle out. The flask was then cooled in a refrigerator for twelve hours, and the precipitate was filtered off and dried. The octa-mercurial was dissolved in glacial acetic acid, boiled with a small amount of charcoal, and filtered hot. The precipitate formed upon cooling was filtered off and dried under vacuum. It decomposed at 320–340°.

Anal. Calcd. for $C_{46}H_{46}O_{20}Hg_8$: Hg, 63.6. Found: Hg, 63.0.

Benzoyl-4,4'-dihydroxy-tritan (II).—One mole (94 g.) of phenol and one-fourth of a mole (52.5 g.) of benzil were placed in a one-liter three-necked round-bottomed flask provided with a gas inlet tube, 100 cc. of glacial acetic acid was added as a solvent, and dry hydrogen

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[8] M. E. McGreal, V. Niederl and J. B. Niederl, THIS JOURNAL, 61, 435 (1939).

[9] P. Papadakis, private communication.

[10] Shukis, A., M.Sc. Thesis, New York University, June, 1940, p. 26.

chloride gas was passed into the reaction mixture at room temperature for six hours. The latter was then tightly stoppered and allowed to stand for ten days. The liquid in this time had become quite viscous and had turned deep red. The mixture was then subjected to steam distillation to free it from unreacted phenol and solvent; the non-volatile residue, which was obtained in the form of a cake, was crushed, dried, and recrystallized from benzene in the form of orange-colored plates. The crystals are soluble in alkali, m. p. 212° (uncor.).

Anal. Calcd. for $C_{26}H_{20}O_3$: C, 82.10; H, 5.26; mol. wt., 380. Found: C, 82.13; H, 5.26; mol. wt., 370.

Acetate (IIa).—Two grams of the condensation product was refluxed for two hours with 25 cc. of acetic anhydride in an all-glass apparatus. The solution was poured into cold water and was allowed to stand, with occasional shaking, till the excess reagent had hydrolyzed. The resulting semi-solid was transferred onto a porous tile till it had completely solidified, then recrystallized from alcohol, m. p. 168° (uncor.).

Anal. Calcd. for $C_{30}H_{24}O_5$: C, 77.58; H, 5.17; mol. wt., 464. Found: C, 77.30; H, 4.91; mol. wt., 461.

Propionate (IIb).—A mixture of two grams of the benzil-phenol condensation product and 25 cc. of propionic anhydride was refluxed for two hours, then poured into cold water and allowed to stand overnight. The resulting solid was recrystallized from alcohol, m. p. 123–125° (uncor.).

Anal. Calcd. for $C_{32}H_{28}O_5$: C, 78.05; H, 5.69. Found: C, 77.90; H, 5.78.

Benzhydryl-4,4′-dihydroxy-tritan (III).—Five grams of the benzil–phenol condensation product was dissolved in 50 cc. of absolute amyl alcohol in a 200 cc. round-bottomed flask provided with a reflux condenser. The solution was heated to boiling and, in the course of a half hour, five grams of freshly cut sodium was added, the mixture being gently refluxed the while. After all the sodium had been added, the solution was allowed to cool, then transferred to a separatory funnel, to which was also added 50 cc. of water and 25 cc. of ether. The mixture was thoroughly shaken and the lower aqueous layer was drawn off. The ether layer was washed with water and the washings added to the main extract, which was then acidified with dilute hydrochloric acid. The acidified mixture was then extracted with 25-cc. portions of ether; the ether extract was evaporated to dryness and the solid obtained was crystallized from benzene. The product is soluble in alkali, m. p. 152–154° (uncor.).

Anal. Calcd. for $C_{26}H_{22}O_3$: C, 81.67; H, 5.78. Found: C, 81.80; H, 5.49.

Acetate (IIIa).—The acetate of the reduced phenol was prepared in the manner previously described. The triacetate was recrystallized from alcohol, m. p. 114–116° (uncor.).

Anal. Calcd. for $C_{32}H_{28}O_6$: C, 75.60; H, 5.52. Found: C, 76.16; H, 5.40.

Summary

This communication concludes the systematic investigation of the condensations of diketones with phenols. In the course of this research tetraphenols, indano-indanes, coumarano-coumarans, tritan, naphthalene and anthracene compounds were produced.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

The Resolution of Racemic Pantothenic Acid by Means of Quinine Methohydroxide

BY ERIC T. STILLER AND PAUL F. WILEY

The syntheses of *dextro-* and *levo-*rotatory pantothenic acid from the optical enantiomorphs of α,γ-dihydroxy-β,β-dimethylbutyric acid have already been described by Stiller, *et al.*[1] In this same paper the preparation of racemic pantothenic acid was also described. In the interim, the resolution of racemic pantothenic acid has been described by Kuhn and Wieland[2] who made use of the corresponding quinine salt.

The present paper deals with the optical resolution of the racemic pantothenic acid by means of a novel reagent.[3]

Preliminary experiments indicated that some of the alkaloidal salts of *dl*-pantothenic acid did not lend themselves to continued recrystallization owing to decomposition. A stronger optically active base was sought which would form a readily crystallizable salt with the racemic acid. Attention was, therefore, turned to the optically active quaternary ammonium hydroxides.

The salt obtained by the neutralization of an aqueous solution of racemic pantothenic acid with an aqueous solution of quinine methohydroxide was crystallized readily from an alcohol–ether mixture.

The least soluble fraction of the quaternary ammonium salt gave, after six recrystallizations, the pure salt of (+)-pantothenic acid ($(\alpha)^{25°}\mathrm{D}$ $-122.0°$; m. p. 197°), in admixture with a

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[1] Stiller, Harris, Finkelstein, Keresztesy and Folkers, THIS JOURNAL, 62, 1785 (1940).

[2] Kuhn, Wieland, *Ber.*, 73, 971 (1940).

[3] Major and Finkelstein, THIS JOURNAL, 63, 1368 (1941).