a M.F.D. of 9.0 mg. Consequently, this form of vitamin E is only one-twelfth as potent, measured by the rat-antisterility test, as α-tocopherol and only about one-fifth as potent as β-tocopherol.

Crystalline α-tocopheryl acid succinate is suggested as a Standard of Reference for vitamin E. The present International Standard, *dl*-α-tocopheryl acetate, recently proposed,[9] is a viscous, oily compound relatively more difficult to purify, duplicate and handle than the crystalline succinic acid ester.[1]

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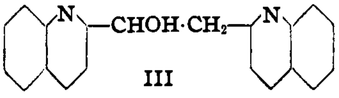
[CONTRIBUTION FROM NICHOLS LABORATORY, NEW YORK UNIVERSITY]

Condensation Reactions of Cinchoninaldehyde and Quinaldaldehyde[1]

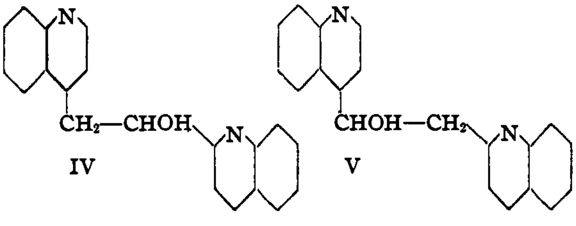
BY HARRY KAPLAN[2] AND H. G. LINDWALL

Earlier studies[3] of quinoline-4-aldehyde (cinchoninaldehyde II) and quinoline-2-aldehyde (quinaldaldehyde I) have been extended by investigations of further condensation reactions.

Quinaldaldehyde (I) has been found to condense with quinaldine and also with lepidine in aqueous alcoholic medium with or without diethylamine as a catalyst. In this way, 1,2-bis-(quinolyl-2)-ethanol-1 (III) and 1-(quinolyl-2)-2-(quinolyl-4)-ethanol-1 (IV) have been obtained, respectively. Under similar conditions, cinchoninaldehyde (II) has been found to yield an aldol-like product with quinaldine, namely, 1-(quinolyl-4)-2-(quinolyl-2)-ethanol-1 (V). The analogous product from II and lepidine could not be obtained.

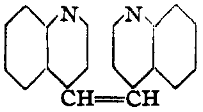


III

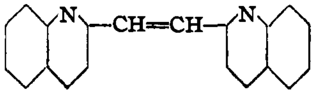


IV V

Lepidine and cinchoninaldehyde heated together in a sealed tube with glacial acetic acid and acetic anhydride, or with anhydrous zinc chloride, gave 1,2-bis-(quinolyl-4)-ethene (VII). Quinaldine and quinaldaldehyde (I) similarly yielded 1,2-bis-(quinolyl-2)-ethene (VI); compound VI was also obtained by the dehydration of compound III through the use of hot glacial acetic acid and acetic anhydride.



VII



VI

Both cinchoninaldehyde (II) and quinaldaldehyde (I) formed anils with sulfanilamide, compound IX from II and VIII from I. Also the respective carbazones of II and I were prepared.

Experimental

1,2-Bis-(quinolyl-2)-ethanol-1 (III).—Quinaldine (0.5 cc.) and quinaldaldehyde (0.5 g.) were dissolved in aqueous alcohol (10 cc. 80% alcohol), with or without 6 drops of diethylamine. After refluxing about 6 hours, III separated from the hot solution; yield 0.75 g. (75%). Recrystallized from ethanol, methanol, or pyridine: m. p. 167–168°.

Anal. Calcd. for $C_{20}H_{16}ON_2$: N, 9.33. Found: N, 9.13.

1-(Quinolyl-2)-2-(quinolyl-4)-ethanol-1 (IV).—A solution of quinaldaldehyde (1 g.) and lepidine (1 cc.) in 15 cc. of aqueous alcohol (80%) with or without 6 drops of diethylamine, was refluxed about six hours. After removal of solvent by distillation under reduced pressure, the residue was recrystallized from pyridine and then from ethanol as practically colorless small flaky crystals; yield, 1.46 g. (73%); m. p. 191–192°.

Anal. Calcd. for $C_{20}H_{16}ON_2$: N, 9.33. Found: N, 9.23.

1-(Quinolyl-4)-2-(quinolyl-2)-ethanol-1 (V).—Cinchoninaldehyde (1 g.) and quinaldine (1 cc.) were dissolved in 2 cc. *n*-propanol, with or without 6 drops of diethylamine, and the reaction mixture was kept at reflux overnight. V precipitated from the reaction mixture, and was recrystallized from ethanol or *n*-propanol; yield 1.44 g. (72%); m. p. 180–182°.

Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 80.0; H, 5.33. Found: C, 79.9; H, 5.16.

Benzoate of V (Va).—V (60 mg.) was dissolved in pyridine (1.5 cc.) and benzoyl chloride (0.2 cc.) was added, as well as sufficient chloroform (0.8 to 1.0 cc.) to dissolve the resultant precipitate. After standing overnight, the reaction mixture was poured into a small amount of dilute sulfuric acid. Va separated as a solid and was recrystal-

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[1] Original manuscript received February 2, 1942.

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[3] (a) Kwartler and Lindwall. THIS JOURNAL. 59, 524 (1937); (b) Kaplan. *ibid.*, 63, 2654 (1941).

lized from ethyl alcohol in the form of shiny white platelets; m. p. 162°. Unaffected by lengthy boiling with sodium carbonate, Va is hydrolyzed by boiling several hours with concentrated hydrochloric acid, benzoic acid being recovered from the reaction mixture.

Anal. Calcd. for $C_{27}H_{20}O_2N_2$: C, 80.2; H, 4.95; N, 6.93. Found: C, 80.3; H, 5.20; N, 7.20.

1,2-Bis-(quinolyl-2)-ethene (VI).—Method A: Quinaldine (0.2 cc.) and quinaldaldehyde (0.2 g.) were sealed into a tube together with glacial acetic acid (0.2 cc.) and a few drops of acetic anhydride and heated at 120° overnight. The reaction mixture was neutralized with ammonia and extracted with ether. Evaporation of the ether left a viscous oil; this was repeatedly dissolved in alcohol which was then allowed to evaporate completely at room temperature. After several days, long flat white crystals appeared; when this occurred, the slight residual amount of alcohol was taken up with filter paper; m. p. 326°.

Method B: For the mixture of glacial acetic acid and acetic anhydride of Method A, 0.2 g. of zinc chloride was substituted. The remainder of the procedure was precisely as in A.

Method C: Compound III (0.4 g.) was refluxed about 3 hours in glacial acetic acid (2 cc.) and a few drops of acetic anhydride. After neutralizing, procedure was as in A above.

1,2-Bis-(quinolyl-4)-ethene (VII).—Method A: Lepidine (0.5 cc.) and cinchoninaldehyde (0.5 g.) were sealed into a tube with glacial acetic acid (1 cc.) and a few drops of acetic anhydride. After being heated overnight at 110°, the reaction mixture was neutralized with ammonia and extracted with ether. VII remained after the ether was evaporated, and was recrystallized from alcohol; yield 0.6 g. (60%); m. p. 207°.

Method B: Zinc chloride was used as the condensing reagent; otherwise the procedure was as in A.

Method C:[3b] VII occurs in quantitative yield when lepidine is oxidized by old selenium dioxide, not sublimed at time of preparation.

Anal. Calcd. for $C_{20}H_{14}N_2$: N, 9.92. Found: N, 10.3.

N^4-(2-Quinolylmethylene)-sulfanilamide (VIII).—To a solution of quinaldaldehyde in *n*-butanol (0.5 g. in 10 cc.) were added in turn 10 cc. of toluene and then a solution of sulfanilamide (0.55 g.) in *n*-butanol (10 cc.). The precipitate that formed shortly was dissolved after refluxing three hours; the reaction mixture was kept at reflux one hour more. On cooling, VIII separated from the solution in fine, pale yellow crystals; yield 0.75 g. (76%); m. p. 188–189° (dec.).

Anal. Calcd. for $C_{16}H_{13}N_3O_2S$: N, 13.5. Found: N, 14.0.

N^4-(4-Quinolylmethylene)-sulfanilamide (IX).—Cinchoninaldehyde (1 g.) and sulfanilamide (1.1 g.) were dissolved in 15 cc. of glacial acetic acid. The reaction mixture was kept at reflux for three hours and was then permitted to cool, precipitating IX. A further quantity of IX was recovered by diluting the acid solution with water. Fine yellow crystals, recrystallized from alcohol; yield 1.4 g. (72%); m. p. 151–153°.

Anal. Calcd. for $C_{16}H_{13}N_3O_2S$: N, 13.5. Found: N, 13.4.

Quinaldaldehyde Semicarbazone (X).—Fine white needles, recrystallized from alcohol; m. p. 232–234° (dec.).

Anal. Calcd. for $C_{11}H_{10}N_4O$: N, 26.14. Found: N, 25.03.

Cinchoninaldehyde Semicarbazone (XI).—Recrystallized from alcohol, fine white needles; m. p. 244–245° (dec.).

Anal. Calcd. for $C_{11}H_{10}N_4O$: N, 26.14. Found: N, 25.82.

Summary

Quinaldaldehyde undergoes the aldol type condensation with quinaldine and lepidine, both with diethylamine and without added catalyst; in the case of cinchoninaldehyde, only the condensation with quinaldine could be effected.

From each aldehyde there has been prepared the unsaturated condensation product with the analogous methyl homolog.

Each of the aldehydes forms a semicarbazone, and each undergoes anil-formation with sulfanilamide.

In all the reactions studied, the expected lesser activity of cinchoninaldehyde as compared with quinaldaldehyde has been observed.

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