gambir by either of the above methods or by the original method of Perkin and Yoshitake[3] using hot ethyl acetate gives a catechin of m. p. 210–213° cor.; $[\alpha]^{26}D$ +14.7°; C = 5% in 50% acetone. The tetramethyl ether and the pentaacetyl ester of this high-melting catechin, however, correspond exactly with those reported by Freudenberg and Purrmann prepared from *d*-catechin, m. p. 174–175°.[2] The rotation and the properties of the derivatives indicate that the catechin thus obtained is chiefly *d*-catechin. Its high melting point indicates that it is either a dimorphic form of *d*-catechin or a mixture of *d*-catechin with small amounts of *dl*-catechin (m. p. 212–214°) or *dl-epi*catechin (m. p. 224–226°). Perkin and Yoshitake[3] obtained a so-called "acacatechin" from acacia or Bengal catechin which melted at 204–205°, and which on careful fractional crystallization by Freudenberg and Purrmann proved to consist chiefly of *l* and *dl*-catechin with small amounts of *l* and *dl-epi*catechin. However, recrystallization of the high melting catechin from *ten* to *twelve* volumes of hot water gives, in almost quantitative yield, the low melting *d*-catechin, m. p. 174–175°, indicating that it is a dimorphic form.

Freudenberg notes that *d*-catechin crystallizes with four molecules of water and melts at 93–95°. The anhydrous product melts at 174–175°. We have found that many samples of *d*-catechin melting at 174–175° and also 210–213° contain water of crystallization (0.1 to 1 mole) depending upon the method of crystallization and the duration and type of drying.

(3) Perkin and Yoshitake, *J. Chem. Soc.*, **81**, 1162 (1902).

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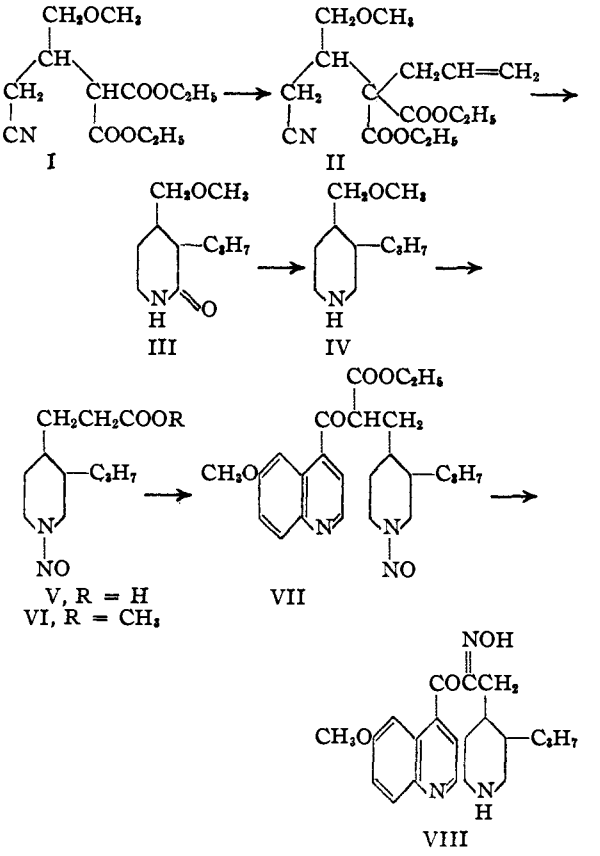
6′-Methoxy-8-oximino-3-propylrubatoxanone

BY C. F. KOELSCH

The experiments described in the present paper were carried out as models for part of a projected synthesis of quinine. Key substances in the series of reactions used[1] are formulated in the accompanying chart. It is indicated that condensation of VI with ethyl quininate yielded VII, but this compound could not be purified. When the condensation product was boiled with hydrochloric acid, it was converted into a crystalline substance which appears to be the dihydrochloride of VIII, a compound whose reduction should yield interesting results. The research, however, was interrupted in 1942, before the reduction could be studied, and in view of the recent synthesis of quinine in another laboratory,[2] no further work on the subject is contemplated.

(1) *Cf.*, Koelsch, THIS JOURNAL, **65**, 2458, 2460 (1943); **66**, 1611 (1944).

(2) Woodward and Doering, *ibid.*, **66**, 849 (1944); **67**, 860 (1945).



Experimental

4,4-Dicarbethoxy-3-methoxymethyl-Δ⁶-heptenonitrile (II).—To a solution of 46 g. of sodium in 550 ml. of dry alcohol were added 320 g. of ethyl malonate and 190 g. of γ-methoxycrotononitrile. The mixture was heated under reflux for ninety minutes, then treated with 25 g. of sodium iodide (dried at 300°) and 160 g. of allyl chloride. Heating was continued for an additional ninety minutes,[3] then most of the alcohol was removed, and water and ether were added. Fractional distillation gave 407 g. (70%), b. p. 192–195° at 19 mm.

Anal. Calcd. for $C_{18}H_{29}NO_5$: C, 60.6; H, 7.7. Found: C, 60.7; H, 7.8.

4-Methoxymethyl-3-propylpiperidone-2 (III).—When a solution of 420 g. of II in 100 ml. of alcohol was reduced with hydrogen at 2200 lb. and 150° using Raney nickel, the calculated amount of hydrogen was absorbed in three and one-half hours. The sirupy product, freed of alcohol, was boiled and stirred for twenty hours with 180 g. of potassium hydroxide in 3500 ml. of water, and the unsaponified part (65 g.) was then removed with ether. The aqueous solution was distilled to about 750 ml., acidified strongly with sulfuric acid, filtered from potassium sulfate, and extracted with five 100-ml. portions of ether. The product, a thick sirup (188 g.) was heated at 185°, giving 158 g. of crude lactam; an additional 22 g. was obtained by distilling the extracted aqueous solution to dryness, combining the residue with the potassium sulfate, and extracting the whole with alcohol. Several fractionations of the crude lactam gave 95 g., b. p. 175–180° at 6 mm.

(3) Orienting experiments indicated that the alkylation was nearly complete after seventy minutes of boiling. When allyl chloride was used without sodium iodide, the alkylation required eight hours. When allyl bromide was used, the reaction mixture required external cooling, and the reaction was complete after less than fifteen minutes. Approximately the same yield of alkylation product was obtained in each of these experiments.

This contained III, as shown by its behavior on reduction, but it gave poor analytical figures for this substance.

Anal. Calcd. for $C_{10}H_{19}NO_2$: C, 64.8; H, 10.3. Found: C, 60.6; H, 9.3.

4-Methoxymethyl-3-propylpiperidine (IV).—The reduction of 100 g. of III with 100 g. of sodium in one liter of dry butyl alcohol gave 43 g. of basic material and 37 g. of neutral material. The latter, a viscous oil with a lard-like odor, represented the impurities in the III used, and gave no definite fraction on distillation, b. p. 140–220° at 8 mm. Distillation of the basic material gave 23 g. of crude piperidine, b. p. 120–135° at 27 mm. This was further purified and possibly separated from a stereoisomer by crystallization of its picrate, yellow needles, m. p. 112–116°, from benzene. After it had been regenerated from the picrate, IV formed a colorless hygroscopic oil (12.6 g.) b. p. 118–122° at 26 mm. It was analyzed as its picrolonate, yellow needles from benzene, m. p. 184–185°.

Anal. Calcd. for $C_{10}H_{21}NO + C_{10}H_8N_4O_5$: C, 55.2; H, 6.7. Found: C, 55.2; H, 6.4.

A solution of 12.5 g. of IV in 125 g. of 51% hydrobromic acid was boiled for six hours. The excess hydrobromic acid was then removed at 100° under reduced pressure, leaving 22 g. of **4-bromomethyl-3-propylpiperidine hydrobromide,** a pale brown sirup.

Anal. Calcd. for $C_9H_{18}Br_2N$: Br, 53.2. Found: Br, 53.2.

When a portion of the hydrobromide was steam distilled from excess dilute sodium hydroxide, it yielded **3-propyl-1-azabicyclo[2,2,1]heptane,** an oil with a sweet fishy odor; the **picrate** formed bright yellow prisms from dilute alcohol, m. p. 129–130°.

Anal. Calcd. for $C_9H_{17}N + C_6H_3N_3O_7$: C, 49.0; H, 5.5. Found: C, 49.2; H, 5.6.

The **picrolonate** formed pale yellow-brown prisms from alcohol, m. p. 204–205°.

Anal. Calcd. for $C_9H_{17}N + C_{10}H_8N_4O_5$: C, 56.6; H, 6.2. Found: C, 57.4; H, 6.6.

1-Nitroso-3-propylpiperidine-4-propionic Acid (V).—A solution of 21.5 g. of 4-bromomethyl-3-propylpiperidine hydrobromide in 25 ml. of water containing a few drops of hydrobromic acid was treated with 6 g. of sodium nitrite, warmed to 70°, and then cooled. The oily nitroso compound was taken up in ether, washed with dilute sodium carbonate, and dried by heating at 100° and 20 mm.; yield 16.6 g. This crude product was added to a solution of 1.6 g. of sodium and 12 g. of ethyl malonate in 20 ml. of alcohol, and the mixture was boiled for one hour. The product (22.2 g.) was boiled for one hour with 7.5 g. of sodium hydroxide in 50 ml. of water, unsaponified material (6.5 g.) was removed with ether, and the solution was acidified and extracted with ether. The resulting **1-nitroso-3-propyl-4-piperidylmethylmalonic acid** was a yellow glass (11.8 g.) that could not be obtained crystalline even after it had been purified through its **calcium salt,** difficultly soluble colorless crystals from water.

Anal. Calcd. for $C_{12}H_{18}N_2O_5Ca + 1.5\ H_2O$: Ca, 11.9; H_2O, 8.0. Found: Ca, 11.6; H_2O, 8.0.

When 9.7 g. of the malonic acid was heated at 150° until frothing stopped, and then cooled, there was obtained 7.9 g. of crystalline V. The product separated from dilute acetic acid in the form of colorless plates, m. p. 106°.

Anal. Calcd. for $C_{11}H_{20}N_2O_3$: C, 57.9; H, 8.8. Found: C, 58.2; H, 9.0.

A solution of 1 g. of V in 3 ml. of concentrated hydrochloric acid was treated with 0.75 g. of cuprous chloride, and after no more nitric oxide was evolved, the mixture was distilled to dryness under reduced pressure and then dissolved in water. Copper was removed with hydrogen sulfide, hydrochloric acid with excess silver oxide, and the resulting easily soluble silver salt was freed of silver with hydrogen sulfide. This gave **3-propylpiperidine-4-propionic acid,** colorless crystals from a mixture of alcohol and ether that were easily soluble in water; it became brown and sintered at 244° and melted with effervescence at 247°.

Anal. Calcd. for $C_{11}H_{21}NO_2$: C, 66.3; H, 10.5. Found: C, 66.5; H, 10.1.

Methyl 1-nitroso-3-propylpiperidine-4-propionate (VI), b. p. 195–197° at 7 mm., was a yellow oil with a furfural-like odor. It was obtained in quantitative yield by the action of diazomethane on the acid, and when a portion of the distilled ester was saponified, it gave back the parent acid.

Anal. Calcd. for $C_{12}H_{22}N_2O_3$: C, 59.9; H, 9.3. Found: C, 59.5; H, 9.1.

Condensation with Ethyl Quininate.—To a suspension of sodium ethoxide from 1 g. of powdered sodium in 25 ml. of ether was added 5.6 g. of ethyl quininate[4] and 5.5 g. of VI. The mixture was heated at 40° in a closed vessel for twenty-four hours, and then allowed to stand at room temperature for two days. It was extracted with dilute sodium hydroxide and then with dilute hydrochloric acid. The material left in the ether was VI (1.9 g.); that removed by hydrochloric acid was ethyl quininate (0.8 g.). The sodium hydroxide extract was acidified with hydrochloric acid, then made slightly basic with sodium carbonate, quininic acid (3.5 g.) dissolving. The pale brown oil (VII, 3.6 g.) remaining gave a deep red color with alcoholic ferric chloride, but no crystalline salt could be obtained from it. It was boiled for one hour with 5 ml. of hydrochloric acid in 10 ml. of water (carbon dioxide evolution), the solution was cooled, and the crystalline product was removed and washed with dilute hydrochloric acid. Precipitated from 95% alcohol with ether, the resulting **dihydrochloride** of VIII formed bulky fine white needles that changed on standing under the mother liquor for one hour into dense pale yellow micro needles (1.25 g.). The salt decomposed above 245°; it gave neither a ferric chloride reaction nor a Liebermann test.[5]

Anal. Calcd. for $C_{21}H_{27}N_3O_3 + 2HCl$: C, 57.0; H, 6.5; N, 9.5. Found: C, 57.3; H, 6.3; N, 10.1.

A solution of 0.75 g. of the dihydrochloride in water was brought to *p*H 8.5 with sodium carbonate. The resulting white precipitate, apparently a carbonate, was nearly insoluble in water but easily soluble in dilute sodium hydroxide. It was removed and dissolved in 8 ml. of hot 3% acetic acid. Cooling this solution gave the **monoacetate** of VIII, which after recrystallization from water formed white needles (0.6 g.) that darkened slightly at 185°, sintered at 195° and melted with blackening and gas evolution at 198°.

Anal. Calcd. for $C_{21}H_{27}N_3O_3 + C_2H_4O_2$: C, 64.4; H, 7.2. Found: C, 64.5; H, 7.2.

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(4) 2-Chloroquininic acid, prepared by the method of Thielepape and Fulde [*Ber.*, **72**, 1432 (1939)], was converted into quininic acid nearly quantitatively when its solution in aqueous sodium hydroxide was shaken with Raney nickel and hydrogen at 35 lb. and 25° for twenty-four hours. The ester was obtained in 86% yield using alcohol and sulfuric acid [*cf.* Cohen and King, *Proc. Roy. Soc.* (London), **B125**, 49 (1938)].

(5) The general properties of VIII were very similar to those described for 6-methoxy-8-oximino-3-vinylrubatoxanone [v. Miller, Rohde and Fussenegger, *Ber.*, **33**, 3234 (1900); Rohde and Schwab, *ibid.*, **38**, 315 (1905)] except that the latter substance was reported to give a Liebermann test. Several other α-diketone monoximes investigated by the present author have been found to give no Liebermann test, and a negative test has been reported in a similar instance by Harries and Groschuff [*Ann.*, **417**, 185 (1918)]. It therefore appears that the positive test obtained by Rohde and co-workers may have been caused by the presence of a small amount of N-nitroso compound in the substance they were investigating.