[Chem. Pharm. Bull. 14(9)1052~1053(1966)]

UDC 547.97 : 582.572.2 : 547.567

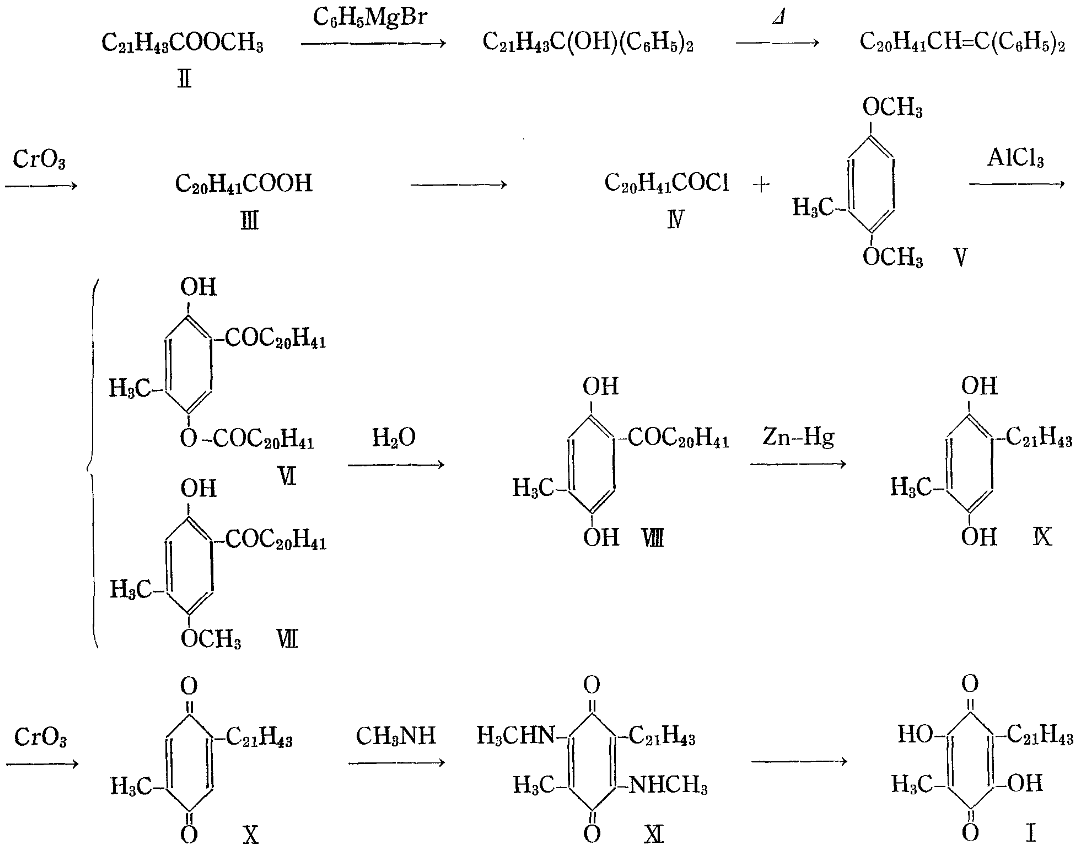
Kunitoshi Yoshihira and Shinsaku Natori :

Synthesis of Polygonaquinone.[*1]

(*National Institute of Hygienic Sciences*[*2])

Nakata, *et al.*,[1] isolated an orange pigment named polygonaquinone from the rhizomes (黄精) of *Polygonatum falcutum* A. Gray (narukoyuri, Liliaceae) and elucidated the structure as 3-heneicosyl-6-methyl-2,5-dihydroxybenzoquinone (I), chiefly from spectroscopic evidences.[2~4] Since further studies on the closely related benzoquinones from Myrsinaceae plants[2] and from molds[3] are under investigation in our laboratory and the structure (I) suffices the conditions to show ubiquinone-like activity,[5] synthetic confirmation of the structure (I) has been attempted.

Following the method of Cruickshank and Robinson,[6] 2,5-dimethoxytoluene (V) was condensed with heneicosanoyl chloride (IV), prepared from behenic acid by Barbier-Wieland degradation and the following chlorination, to obtain a mixture of 2-hydroxy-



[*1] The content of this paper was presented at the Annual Meeting of the Pharmaceutical Society of Japan (Tokushima, October 1965).

[*2] Tamagawayoga, Setagaya, Tokyo (義平邦利, 名取信策).

1) H. Nakata, K. Sasaki, I. Morimoto, Y. Hirata : Tetrahedron, **20**, 2319 (1964).

2) H. Ogawa, S. Natori : This Bulletin, **13**, 511 (1965).

3) S. Natori, H. Ogawa, H. Nishikawa : *Ibid.*, **12**, 236 (1964).

4) B.W. Bycraft, J.C. Roberts : J. Org. Chem., **28**, 1429 (1963).

5) H. Ozawa, K. Momose, R. Natori, H. Ogawa, K. Yamaguchi : Biochem. Biophys. Acta, **86**, 395 (1964); H. Ozawa, S. Natori, K. Momose : This Bulletin, **13**, 1029 (1965).

6) J.H. Cruickshank, R. Robinson : J. Chem. Soc., **1938**, 2064; H. Hasan, E. Stedman : *Ibid.*, **1931**, 2112; M. Asano, J. Hase : Yakugaku Zasshi, **60**, 650 (1940); K. Yamaguchi : *Ibid.*, **70**, 241 (1950).

5-heneicosanoyloxy-(VI) and 2-hydroxy-5-methoxy-4-methylheneicosanophenone (VII). The hydrolysis of the former, followed by the Clemmensen reduction, afforded 4-heneicosanyl-2,5-dihydroxytoluene (IX). Oxidation of the hydroquinone afforded the quinone (X), to which two hydroxyl groups were introduced through the bis(methylamino) derivative (XI). The synthetic specimen was proved to be identical with polygonaquinone in every respects. Since no ambiguity remains on the relative positions of the alkyl and hydroxyl groups on benzoquinone nucleus from the reaction course and from the spectral evidences,[7] this synthesis confirms the structure of polygonaquinone (I) and proves the applicability of the empirical rule of infrared and ultraviolet absorptions on the locations of hydroxyl groups on benzoquinone uncleus, proposed by Roberts[4] and by the authors.[2,3] Biochemical examination of the compound with related compounds is now in progress.

Experimental*3

Heneicosanic Acid (III)——Ethereal solution of methyl behenate (II) (6.0 g.) was added to Grignard reagent, prepared from bromobenzene (5.9 g.) and Mg (1.1 g.) in ether. After refluxing for 1 hr., the reaction mixture was decomposed with conc. HCl, the ethereal layer separated, and evaporated. The diphenylcarbinol thus obtained was heated at 150° for 30 min. and recrystallized from acetone to colorless needles (8.2 g.) of 1,1-diphenyl-1-docosene, m.p. 39~40°. *Anal.* Calcd. for $C_{34}H_{52}$: C, 88.62; H, 11.38. Found: C, 88.77; H, 11.45.

The hydrocarbon (5.5 g.) in AcOH (100 ml.) was oxidized with CrO_3 (2.4 g.) in H_2O. After warming on a water bath for 10 min., water was added and the precipitates were collected and recrystallized from EtOH-petr. ether to colorless needles (3.1 g.) of m.p. 68~70°.

2-Hydroxy-5-methoxy- and 2,5-Dihydroxy-4-methylheneicosanophenone (VII and VIII)——To the mixture of heneicosanoyl chloride (IV), prepared from the acid (III) (3.0 g.), $AlCl_3$ (1.5 g.), and CS_2 (20 ml.), 2,5-dimethoxytoluene (1.3 g.) in CS_2 (20 ml.) was added and heated under reflux for 20 hr. The solvent was removed, the residue was treated with 2*N* HCl, and the reaction mixture was extracted with ether. Evaporation of ether and recrystallization from EtOH afforded pale yellow plates (VII) (2.4 g.) of m.p. 82~83°. IR cm^{-1}: 1632 (bonded C=O), 1238 (CH_3O). *Anal.* Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28. Found: C, 78.19; H, 11.59.

From the mother liquor, after further purification from 70% EtOH, yellow needles (VI) of m.p. 45~48° (0.58 g.) were obtained. IR cm^{-1}: 1755 (ester C=O), 1635 (bonded C=O). Hydrolysis of the ester ketone (VI) with EtOH-conc. HCl (1:1) for 8 hr. afforded yellow needles (VIII) (0.5 g.) of m.p. 95~97° from hexane. IR cm^{-1}: 3290 (OH), 1650 (bonded C=O). *Anal.* Calcd. for $C_{28}H_{48}O_3$: C, 77.72; H, 11.18. Found: C, 77.71; H, 11.26.

4-Heneicosyl-2,5-dihydroxytoluene (IX)——To VI or VIII (0.5 g.) and amalgamated Zn (5.0 g.) in EtOH (100 ml.) was added conc. HCl (5 ml.) under refluxing and stirring. After 10 hr., the reaction mixture was filtered while hot and the filtrate was concentrated. Further purification from EtOH afforded colorless needles (0.21 g.) of m.p. 51~53°. IR cm^{-1}: 3240 (OH). *Anal.* Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.04. Found: C, 79.71; H, 12.43.

2-Heneicosyl-5-methylbenzoquinone (X)——IX (0.15 g.) in AcOH (20 ml.) was oxidized with CrO_3 (0.05 g.) in water (0.1 ml.). After slight warming on a water bath, water was added to form precipitates, which were recrystallized from EtOH to pale yellow plates (0.07 g.) of m.p. 84~85°. IR cm^{-1}: 1652 (C=O). *Anal.* Calcd. for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 80.63; H, 11.88.

2-Heneicosyl-5-methyl-3,6-bis(methylamino)-benzoquinone (XI)——X (0.05 g.) in EtOH was treated with CH_3NH_2 (0.03 g.) in EtOH for 20 hr. The precipitates, separated from the reaction mixture, was filtered off and washed well with EtOH. Red-violet needles (0.04 g.) melted at 125~127°. *Anal.* Calcd. for $C_{30}H_{54}O_2N_2$: C, 75.89; H, 11.47. Found: C, 75.53; H, 11.08.

3-Heneicosyl-6-methyl-2,5-dihydroxybenzoquinone (Polygonaquinone) (I)——XI (0.03 g.) in AcOH (3 ml.) was boiled with 50% H_2SO_4 (3 ml.) for 30 min. After cooling, precipitates were collected and purified from EtOH to give orange-yellow plates (0.01 g.) of m.p. 134~135°. IR cm^{-1}: 3390 (OH), 1615 (C=O). Mixed fusion with the authentic specimen from ***Polygonatum falcutum*** showed no depression of melting point and infrared and ultraviolet spectra and thin-layer chromatography also showed the identity.

The authors thanks are due to Professor Y. Hirata, Nagoya University for his kind donation of the specimen of natural polygonaquinone.

(Received January 21, 1966)

---

*3 Melting points were determined on a Yanagimoto micromelting point apparatus. Infrared spectra were taken on a Koken IRS spectrophotometer in Nujol mull unless otherwise specified.

7) K. Yoshihira, S. Natori: This Bulletin, to be published.