sample of 3-indazolone[2] on TLC. After extraction of hydrolysate with $CHCl_3$, over half of fluorescence remained in aqueous layer and the identification for these material is in progress.

Other experiments in which the urines were extracted with ethyl acetate gave a crystalline metabolite, mp 167—168° (uncorr.). Its mass spectrum was *m/e* 224 (M^+). The NMR spectrum in $CDCl_3$ showed chemical shifts, 4.72 (2H, singlet, $>NCH_2-$) and 5.20 (1H, singlet, -OH or >NH). These data were identical with those of authentic sample of 1-benzylindazolone (BI).[2] TLC of ethyl acetate extract gave another spot. This metabolite was also purified by TLC. Its mass spectrum was *m/e* 219 (M^+) and NMR spectrum in $CDCl_3$ was the τ values being 5.90 (1H, singlet, -OH or >NH) and 2.30 (1H, singlet, -OH or >NH). These data indicated that this metabolite should be desbenzylated BZY (desbenzyl-BZY).

The following scheme is proposed as the metabolic pathway of BZY.

Acknowledgement We are grateful to Dr. Silvestrini, Angelini, Italy, for his kind gift of benzydamine derivatives, and to Daiichi Seiyaku Co. and to Yoshitomi Seiyaku Co. for their kind supply of benzydamine.

Faculty of Pharmaceutical Sciences,
Nagasaki University
Bunkyo-machi, Nagasaki,
852, Japan

SEIGO KATAOKA
KAZUHIKO TAIRA
EIGO TAKABATAKE

Received April 19, 1971

[Chem. Pharm. Bull. 19(7)1513—1514(1971)]

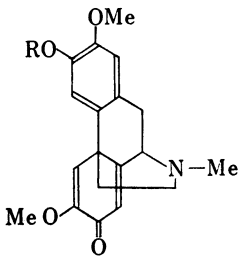
UDC 547.94.07 : 547.833.04

Total Synthesis of Flavinantine and Bracteoline by a Photo-Pschorr Reaction

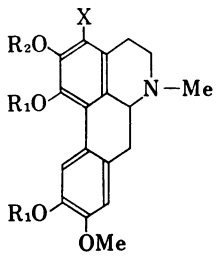
Previously,[1] we reported a total synthesis of flavinantine (I) by debenzylation of the morphinandienone (II), which was obtained by a modified Pschorr reaction[2-4] of the aminoisoquinoline (III) derived from the 1-(2-nitrobenzyl)-isoquinoline (IV). The nature of the reaction of the above synthesis, however, possessed fundamental defects. The first one was regarding the reduction of IV to the aminoisoquinoline (III); the debenzylation occurred as a side reaction and, therefore, it was necessary to separate III from by-products. The second defect was that, in the debenzylation of II to flavinantine (I), several rearranged products were obtained because the morphinandienone was unstable in acid. Therefore, we examined the modified synthesis of the morphinandienone alkaloids. Herein we wish to report total synthesis of flavinantine and bracteoline by a photo-Pschorr reaction.[5]

The nitration of O,O-dibenzylorientaline (V),[6] followed by the reduction of the 2′-nitrobenzylisoquinoline (VI) with zinc and hydrochloric acid, gave the corresponding amino-derivative. Debenzylation of this product in boiling hydrochloric acid, followed by separation as usual, gave 6′-aminoorientaline (VII).

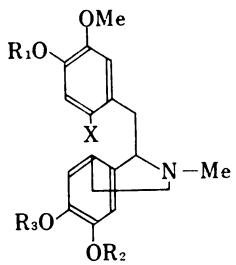
1) T. Kametani, T. Sugahara, H. Yagi, and K. Fukumoto, *J. Chem. Soc.* (*C*), **1969**, 1063.
2) T. Kametani, K. Fukumoto, F. Satoh, and H. Yagi, *J. Chem. Soc.* (*C*), **1969**, 520.
3) T. Kametani, K. Fukumoto, and T. Sugahara, *J. Chem. Soc.* (*C*), **1969**, 801.
4) T. Kametani, M. Ihara, K. Fukumoto, and H. Yagi, *J. Chem. Soc.* (*C*), **1969**, 2030.
5) T. Kametani, K. Fukumoto, and K. Shishido, *Chem. Ind.* (London), **1970**, 1566.
6) A.R. Battersby, T.H. Brown, and J.H. Clements, *J. Chem. Soc.*, **1965**, 4550.



I: R=H
II: R=$CH_2C_6H_5$



IX: R_1=X=H, R_2=Me
XI: R_1=Me, R_2=H, X=NO_2



III: R_1=$CH_2C_6H_5$, R_2=R_3=Me, X=NH_2
IV: R_1=$CH_2C_6H_5$, R_2=R_3=Me, X=NO_2
V: R_1=R_2=$CH_2C_6H_5$, R_3=Me, X=H
VI: R_1=R_2=$CH_2C_6H_5$, R_3=Me, X=NO_2
VII: R_1=R_2=H, R_3=Me, X=NH_2
VIII: R_1=R_2=H, R_3=Me, X=N_2^+
X: R_1=R_2=Me, R_3=H, X=N_2^+

Chart 1

The diazotization of VII as usual,[1-4] followed by irradiation of the resulting diazonium salt (VIII) in diluted sulfuric acid with a Hanovia 450 W mercury lamp at 5—10° using a pyrex filter, gave two products. One of them, obtained in 2% yield, was flavinantine (I), which was identical with the authentic sample[1] according to spectroscopic data. The other one, $C_{19}H_{21}O_4N$ (M^+, *m/e* 327 and microanalysis), mp 210—211°, in 2% yield was shown by the ultraviolet (in MeOH) (270, 279, and 305 nm, log ε 3.94, 4.03 and 4.08), nuclear magnetic resonance (NMR) (τ in $CDCl_3$) [7.84 (NMe), 6.14 (2×OMe), 3.52 (C_3-H), 3.30 (C_8-H) and 2.03 (C_{11}-H)] and mass (*m/e* M^+ 327, 326, 312, 310, 296, 284, 269, 253) spectra[7] to be the 1,2,9,10-tetraoxygenated aporphine system. Therefore, this product was assigned to bracteoline (IX), an alkaloid from *Papaver bracteatum*.[8] It is interesting that the thermal decomposition of the diazotized phenolic isoquinoline (X) gave the nitro-derivative (XI), an unusual product, as a main product,[9] but not in a photo-Pschorr reaction.

Thus, we achieved the total synthesis of flavinantine and bracteoline by a photo-Pschorr reaction.

Acknowledgement We thank Miss A. Kawakami, Miss C. Yoshida, Miss Y. Tadano, Miss T. Yoshida, and Miss R. Kato for the microanalyses.

Pharmaceutical Institute,
Tohoku University
Aobayama, Sendai

Tetsuji Kametani
Hideo Sugi
Shiroshi Shibuya
Keiichiro Fukumoto

Received February 20, 1971

7) S. Shamma and W.A. Slusarchyk, *Chem. Revs.*, **64**, 59 (1964).
8) K. Heydenreich and S. Pfeifer, *Pharmazie*, **22**, 124 (1967).
9) T. Kametani, K. Takahashi, T. Sugahara, M. Koizumi, and K. Fukumoto, *J. Chem. Soc.* (*C*), **1971**, 1032.