derivatives were found to be active. The optimum concentrations were rather lower than the expected ones from the relationship between the optimum concentration for shoot formation and that for promotion of cell division by 4PU derivatives and purine cytokinins. In particular, 4-benzylamino-6-methylaminopyrimidine (**5**), 4-benzoylamino-6-chloropyrimidine (**6**), and 4-chloro-6-isopentenylaminopyrimidine (**7**) were active at the same concentration as the optimum concentration for promotion of cell division in the absence of added auxin. 4-Benzylaminopyrimidine (**8**) which did not promote cell division showed a weak activity in the shoot formation experiment.

In summary, most of cytokinin-active pyridylureas and aminopyrimidines were proved to be active in the shoot formation of tobacco callus.

Experimental Station for Medicinal Plant Studies, Faculty of Pharmaceutical Sciences, University of Tokyo,
1479, Hatakemachi, Chiba-shi, Chiba
TOSHIHIKO OKAMOTO
KOICHI SHUDO

Laboratory of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, University of Tokyo,
Hongo, Bunkyo-ku, Tokyo
SOSHIRO TAKAHASHI
TAKASHI YATSUNAMI

Department of Biology, College of General Education, University of Tokyo,
Komaba, Meguro-ku, Tokyo
YO ISOGAI
KUMIKO YAMADA

Received July 6, 1978

[Chem. Pharm. Bull. 26(10)3252—3254(1978)]

UDC 547.978.04.057 : 547.833.6.04

Sanguirubine and Sanguilutine[1)]

Structures of sanguirubine (3) and sanguilutine (4), a fully aromatized O_5-benzo[*c*]phenanthridine alkaloid, were established by synthesis through a newly developed pathway.

Keywords——O_5-benzo[*c*]phenanthridine alkaloid; synthesis; structural establishment; Bischler–Napieralski reaction; sanguirubine; sanguilutine

The natural occurrence[2)] of four fully aromatized O_5-benzo[*c*]phenanthridine alkaloids has been known in *Papaveraceous* plants. We succeeded in establishing the structures of chelirubine[3)] (**1**) and chelilutine[4)] (**2**) by the syntheses of them and proposed tentative structures of sanguirubine[5)] (**3**) and sanguilutine[5)] (**4**) from diagnostic inspection of the reported NMR

[1)] This paper forms Part XXXIX of "Studies on the Chemical Constituents of *Rutaceous* Plants" by H. Ishii. Part XXXVIII; H. Ishii and T. Ishikawa, *Chem. Pharm. Bull.* (Tokyo), **26**, 2598 (1978).

[2)] F. Šantavý, "The Alkaloids," ed. by R.H. Manske, Academic Press, New York and London, 1970, Vol. 12, p. 333.

[3)] *a*) H. Ishii, K.-I. Harada, T. Ishida, E. Ueda, K. Nakajima, I. Ninomiya, T. Naito, and T. Kiguchi, *Tetrahedron Lett.*, **1975**, 319; *b*) H. Ishii, E. Ueda, K. Nakajima, T. Ishida, T. Ishikawa, K.-I. Harada, I. Ninomiya, T. Naito, and T. Kiguchi, *Chem. Pharm. Bull.* (Tokyo), **26**, 864 (1978).

[4)] H. Ishii, T. Ishikawa, Y.-I. Ichikawa, and M. Sakamoto, *Chem. Pharm. Bull.* (Tokyo), **25**, 3120 (1977).

[5)] *a*) J. Slavík and L. Slavíková, *Collect. Czech. Chem. Commun.*, **25**, 1667 (1960); *b*) J. Slavík, L. Dolejš, V. Hanuš, and A.D. Cross, *Collect. Czech. Chem. Commun.*, **33**, 1619 (1968).

spectral data.[5b] In this communication, we wish to report total synthesis of sanguirubine[5] (**3**) and sanguilutine[5] (**4**) *via* a newly developed pathway,[4] indicating the validity of our proposal for these two alkaloids.

According to the well-known synthetic pathway[6] in the chemistry of benzo[*c*]phenanthridine alkaloids, the starting tetralone derivatives were prepared. Aldol condensation of acetoveratrone[7] (**5**) with 2-methoxy-4,5-methylenedioxy-[8,9] (**6a**) and 2,4,5-trimethoxy-[9,10] (**6b**) benzaldehyde gave the corresponding chalcones[11] [**7a**: mp 173—174° and **7b**: mp 138—142°], which were subjected to hydrocyanation to give the keto-nitriles[11] [**8a**: mp 156—158° and **8b**: mp 154—156°]. Treatment of these nitriles (**8**) with H_2SO_4 in AcOH followed by hydrogenolysis provided the amides[11] [**9a**: mp 131—132° and **9b**: mp 119—121°], which were hydrolyzed by *ca.* 20% KOH in EtOH to give the acids[11] [**10a**: mp 114—117° and **10b**: oil, bp 265—270° (1 mmHg)]. Treatment of these acids (**10**) with $POCl_3$ gave the starting tetralones[11] (**11**) in 54.7% [**11a**: mp 209—211°] and 53.0% [**11b**: mp 152—154°] yields from the corresponding chalcones (**7**).

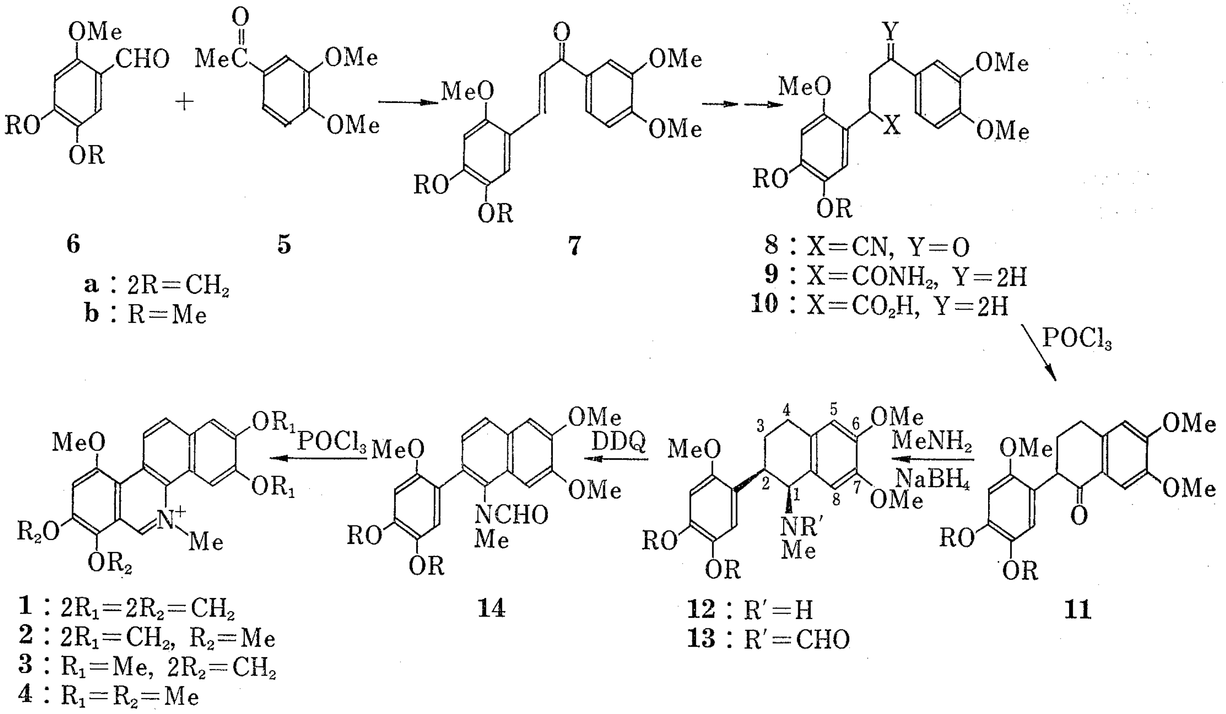

Chart 1

These tetralones (**11**) were treated with CH_3NH_2 and $TiCl_4$ in $CHCl_3$ followed by reduction with $NaBH_4$ to give the corresponding monomethyl amine products[11] [**12a**: mp 147—149° and **12b**: mp 144—146°] as a sole product.

We[12] accomplished the studies on the *J* value of the C_1–H in the NMR spectra of diastereomeric pairs of 2-phenyl-1,2,3,4-tetrahydro-1-naphthylamine derivatives and found

---

6) *a*) T. Richardson, R. Robinson, and E. Seijo, *J. Chem. Soc.*, **1937**, 835; A.S. Bailey and R. Robinson, *J. Chem. Soc.*, **1950**, 1375; *b*) K.-Y. Zee-Cheng and C.C. Cheng, *J. Heterocyclic Chem.*, **10**, 85 (1973).

7) E. Neizel, *Ber.*, **24**, 2863 (1891).

8) K. Fukui and M. Nakayama, *Nippon Kagaku Zasshi*, **84**, 606 (1963).

9) H. Ishii, K.-I. Harada, T. Deushi, E. Ueda, T. Ishida, M. Sakamoto, T. Watanabe, Y.-I. Ichikawa, K. Nakajima, K. Takizawa, and E. Kawanabe, *Chem. Pharm. Bull.* (Tokyo), in preparation.

10) L. Gattermann and F. Eggers, *Ber.*, **32**, 289 (1899).

11) The compound gave satisfactory elemental analysis and the structure was supported by spectral data (NMR, IR, and MS).

12) H. Ishii, T. Deushi, M. Sakamoto, T. Ishida, K.-I. Harada, and T. Ishikawa, *Chem. Pharm. Bull.* (Tokyo), in preparation.

that the C_1-H of the *cis* compound has 3—5 Hz of a J value but that of the *trans* 10—12 Hz. The fact that the signal[12] due to the C_1–H of these products (**12**) appears at δ 3.70 as a doublet having about 4 Hz of a J value allowed us to assign the configuration of them to be *cis*.

Refluxing these products (**12**) with chloral in $CHCl_3$ afforded 1,2,3,4-tetrahydro-1-naphthylformamides[11] (**13**) in 83.0% [**13a**: mp 182.5—185°] and 87.0% [**13b**: mp 161—162°] yields. Dehydrogenation of these formamides (**13**) with DDQ gave the fully aromatized formamides[11] (**14**) in 84.9% [**14a**: mp 217—219°] and 80.6% [**14b**: mp 211—215°] yields.

Bischler–Napieralski reaction of the trimethoxy-formamide (**14a**) with $POCl_3$ in xylene afforded red needles, mp 281—284° (lit.[5a] mp 275—276°) in 42.4% yield, which was identified with an authentic sample of sanguirubine[5] (**3**) chloride.

On the other hand, treatment of the pentamethoxy-formamide (**14b**) with $POCl_3$ in CH_3CN gave orange needles, mp 140—145° (dec.) (lit.[5a] mp 163—164°) in 60.8% yield, which was identified with an authentic sample of sanguilutine [5] (**4**) chloride. This material was also characterized as ψ-cyanide (**15**), mp 228—232° (lit.[5a] mp 232—233°).

Acknowledgement We wish to thank Prof. J. Slavík, Purkyně University, for the gift of the samples of sanguirubine chloride and sanguilutine chloride.

Faculty of Pharmaceutical Sciences,
Chiba University, 1-33, Yayoi-cho,
Chiba, 260, Japan

HISASHI ISHII
TOSHIKO WATANABE[13]
TSUTOMU ISHIKAWA

Received July 15, 1978

---

[13] Present address: *School of Pharmaceutical Science, Toho University, 2-2-1, Miyama, Funabashi, 274 Japan.*

[Chem. Pharm. Bull. 26(10)3254—3256(1978)]

UDC 547.786.057 : 547.232.04

Synthesis of Isoxazole Derivatives by Means of O-Acylation of Aliphatic Nitro Compounds in the Presence of Acetylenic Compounds[1]

O-Acylation of some aliphatic nitro compounds or their alkali metal salts with acid chlorides in N,N-dimethylacetamide in the presence of acetylenic compounds afforded isoxazole derivatives in fairly good yield. The reaction is shown to arise from 1,3-dipolar cycloaddition of acetylenic compounds to the nitrile oxide intermediates which would resulted from the fragmentation of the initially formed O-acylated product.

Keywords——isoxazole; aliphatic nitro compounds; nitrile oxide; acetylenic compounds; dipolar aprotic solvent; O-acylation; fragmentation; 1,3-dipolar cycloaddition

Several examples have been reported of the O-acylation of aliphatic nitro compounds in which stable nitronic carboxylic anhydrides (mixed anhydrides) are formed from secondary nitroalkanes with acylating agents, while in the case of primary nitroalkanes, the correspond-

---

[1] The Synthetic Reactions of Aliphatic Nitro Compounds. Part XIII: Presented at the 37th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1978: Abstracts, II, p. 731: Part XII of this series: E. Kaji, H. Kohno, and S. Zen, *Bull. Chem. Soc. Jpn.*, **50**, 928 (1977).