HETEROCYCLES, Vol. 29, No. 11, 1989

SYNTHESIS AND CRYSTAL STRUCTURE OF NAPHTHO[2,1-b][1,5]NAPHTHYRIDINE

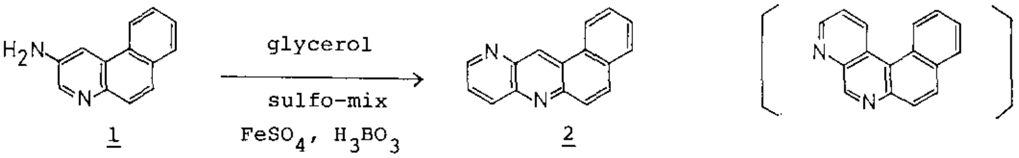
Isao Takeuchi and Yoshiki Hamada*
Faculty of Pharmacy, Meijo University,
Yagoto-Urayama, Tempaku-cho, Tempaku-ku, Nagoya 468, Japan
Kimio Okamura
Research Laboratories of Organic Chemistry, Tanabe Pharmaceutical
Co. Ltd., 2-2-50 Kawagishi, Toda 335, Japan

Abstract —— A modified Skraup reaction was carried out on 2-aminobenzo[f]quinoline (1), in the presence of sulfo-mix, using ferrous sulfate and boric acid. This reaction gave the linear type product, naphtho[2,1-b][1,5]naphthyridine (2), but not the angular type. Its crystal structure was determined by X-ray analysis.

We previously developed a modified Skraup reaction for the syntheses of several nitrogen-containing heterocyclic compounds and reported their chemical reactivity.[1] For example, 1,5-, 1,6-, and 1,8-naphthyridines and 1,6- and 4,6-phenanthrolines in two- or three-ring systems were synthesized in higher yields than those reported previously.[1a,b] We successfully conducted the synthesis of benzo[b][1,8]naphthyridine[1b] for the first time in this study.[2] The syntheses of four-ring systems by the Skraup reaction have not been adequately pursued, and their chemical reactivities of paticular interest in regard to carcinogenic activity.[3] The Skraup reaction was thus carried out on three-ring systems and linear type products were obtained. Structures were assigned on the basis of uv and ^{1}H-nmr spectra and the results of X-ray crystal analysis.

RESULTS AND DISCUSSION

Synthesis of the starting material, 2-aminobenzo[f]quinoline (1),[4] has already been developed at our laboratory by reaction of benzo[f]quinoline with bromo cyanide, followed by bromination and amination. The Skraup reaction of 1 with glycerol was conducted in the presence of sulfo-mix,[5] ferrous sulfate, and boric acid, and a substance (2) with a molecular formula of $C_{16}H_{10}N_2$, m/z 230 (M^+), mp 160-162°C (11.5%) was obtained. (Scheme 1)



linear type angular type

Scheme 1

Product 2 was a four-ring system for whose structure, the linear type or angular type is a possibility. The Skraup reaction of 2-aminophenanthrene produced only the angular type naphtho[1,2-*f*]quinoline.[6] The uv spectra of the linear and angular types showed charactalistic absorptions[7] and the uv spectra of both types for 2 were thus compared for structural assignment.

UV SPECTRUM

In Figure 1, the uv spectrum of 2 is compared with linear (1,2-benzanthracene) and angular types (3,4-benzphenanthrene). Since these types are similar, 2 was considered to be naphtho[2,1-*b*][1,5]naphthyridine.

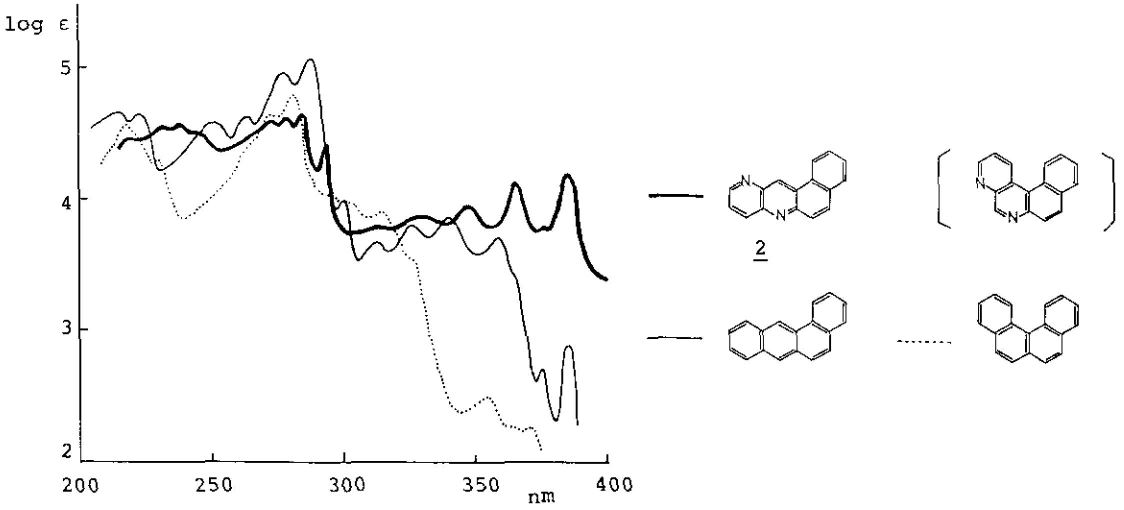
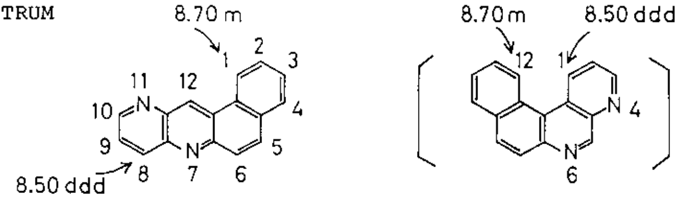


Figure 1. Ultraviolet absorption spectra of 2, 1,2-benzanthracene, and 3,4-benzphenanthrene in cyclohexane.

^{1}H-NMR SPECTRUM



2 linear type

angular type

Scheme 2

The structure of 2 was assigned as the linear type based on its ^{1}H-nmr spectrum. (Scheme 2). Its structure would not be the angular type since such an assignment dose not agree with its structure in that the 1-position proton (δ 8.50) must be situated in the lowest magnetic field. This consideration is based on the ^{1}H-nmr spectrum of angular type naphtho[1,2-*f*]quinoline.[8]

X-RAY CRYSTAL STRUCTURE DETERMINATION OF 2

The structure of 2 appeared to be the linear type based on uv and ^{1}H-nmr spectra and consequently this compound was subjected to X-ray analysis. Its structure 2 was definitely determined as naphtho[2,1-*b*][1,5]naphthyridine. This is the first instance of structural determination for a linear type compound when the Skraup reaction indicates two possibilities for ring formation.

The atomic parameters, atomic nomenclature, bond lenghths and bond angles are given in Table I, Figure 3, and Figure 2. All structural atoms can be seen to lie on the same plane within experimental errors.

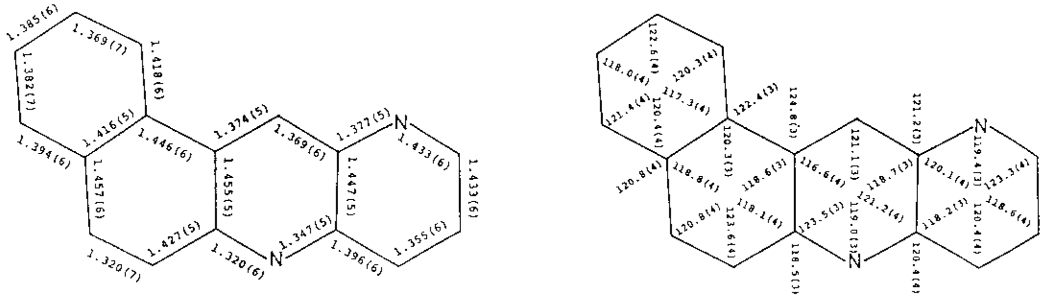


Figure 2. Bond lengths (Å) and bond angles (°) with e.s.d. in parentheses.

EXPERIMENTAL

The ^1H-nmr spectrum of 2 was recorded using JEOL JNM PS-100 spectrometer. Chemical shifts are given in ppm from tetramethylsilane (TMS) as the internal standard, and coupling constants are given in Hz (s, singlet; d, doublet; dd, double doublet; ddd, double double doublet; m, multiplet). Mass spectra was taken with a Hitachi GC-MS M-52 spectrometer. Ir and uv spectra were recorded on JASCO IRA-I and Shimadzu UV-240 spectrophotometer.

Naphtho[2,1-*b*][1,5]naphthyridine (2)

A mixture of sulfo-mix[5] (prepared from 11.9 g of $H_2SO_4 \cdot SO_3$ (20%), and 2.7 g of nitrobenzene), 0.35 g of $FeSO_4 \cdot 7H_2O$, and 0.6 g of H_3BO_3 was chilled to 0-5°C, and 3.1 g of anhyd. glycerol were added to the mixture, followed by the addition of 1.94 g of 2-aminobenzo[*f*]quinoline (1)[4] and 5 ml of warm water (50°C). The mixture was stirred at 130°C for 5 h. The reaction mixture was neutralized with 28% NH_4OH and the resulting precipitate was filtered, the aqueous layer extracted with $CHCl_3$, and the precipitate extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$, the solvent was evaporated, and the residue recrystallized from cyclohexane to give 0.265 g (11.5%) of 2 as yellow needles, mp 160-162°C. Anal. Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 82.94; H, 4.02; N, 12.04. Ms m/z: 230 (M^+); ir ν(KBr) cm^{-1}: 3020, 1600, 1502, 1445, 912, 828, 768, 743; nmr ($CDCl_3$) δ: 7.54-7.88 (3H, m, C_2-H), 7.66 (1H, dd, C_9-H, J=8.6, 3.6 Hz), 7.92 (2H, s, $C_{5,6}$-H), 8.50 (1H, ddd, C_8-H, J=8.6, 1.6, 0.8 Hz), 8.70 (1H, m, C_1-H), 9.04 (1H, dd, C_{10}-H, J=3.6, 1.6 Hz), 9.55 (1H, s, C_{12}-H).

X-Ray crystallography

Formula : $C_{16}H_{10}N_2$, Mw : 230.27

A single crystal of brown transparent needles with dimensions of 0.50 x 0.40 x 0.25 mm^3 was used for data on AFC/5 diffractometer. The lattice constants were determined from angular settings of 25 reflections (2θ values in the range of 30-60°). Crystal data are as follows: a=25.511(3), b=4.957(1), c=17.991(2)Å, β=100.00(1)°, U=2240.7(4)-$Å^3$. Crystal system: monoclinic, Space group C2/c, Z=8, Dx=1.37g/cm^3, F(000)=960, μ(Cu kα)=6.52 cm^{-1}. 1906 unique reflections ($2\theta \leqq 130°$) were measured and 1599 of which with $Fo \geqq 2.67\sigma(Fo)$ were considered actually observable. No absorption corrections were made. The structure was solved by direct methods using MULTAN 80[9] and the difference

Fourier method. More accurate determinations of atomic parameters were made using block-diagonal least-squares methods with anisotropic temperature factors. All hydrogen atoms were shown to be located on difference-Fourier maps and were refined with isotropic temperature factors, while minimizing the function, $\Sigma w(|Fo|-|Fc|)^2$. The weight of $\sqrt{W}=1/\sigma(Fo)$ was used during final refinement. The atomic scattering factors were taken from "International Tables for X-ray crystallography"[10]. The final R value was 0.079 (Rw=0.069).

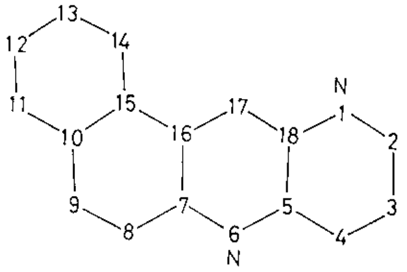


Figure 3. Atomic nomenclature

Table I. Fractional atomic coordinates (x10^4) and equivalent isotropic thermal parameters for non H-atoms with e.s.d. in parentheses.

Atom	No	X	Y	Z	Beq
N	1	658(1)	6852(8)	4266(2)	5.02
C	2	827(2)	8655(10)	3836(2)	5.28
C	3	1379(2)	9230(11)	3853(2)	5.36
C	4	1745(2)	7882(10)	4353(2)	5.06
C	5	1585(1)	5905(8)	4819(2)	4.11
N	6	1948(1)	4525(7)	5308(2)	4.47
C	7	1782(1)	2663(9)	5738(2)	4.12
C	8	2170(1)	1209(10)	6252(2)	5.21
C	9	2049(2)	-698(10)	6706(2)	5.16
C	10	1497(2)	-1423(9)	6714(2)	4.48
C	11	1369(2)	-3467(10)	7184(2)	5.18
C	12	847(2)	-4194(11)	7189(2)	5.66
C	13	450(2)	-2825(11)	6713(2)	5.79
C	14	556(2)	-801(10)	6243(2)	4.99
C	15	1089(1)	-37(9)	6224(2)	4.22
C	16	1224(1)	2041(9)	5725(2)	3.95
C	17	860(1)	3483(9)	5226(2)	4.18
C	18	1021(1)	5397(9)	4765(2)	4.11

ACKNOWLEDGEMENT

The authors are grateful to the members of the Analysis Center of this University for elemental analyses.

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Received, 6th July, 1989