Table 1. Selected ^1H NMR Data for Isocitreoviridin

C#	δ ^1H[a]	COSY[b]
6	5.86, s	
8	6.34, d, $J_{8,9}$=14.40 Hz	H9
9	6.45, dd, $J_{8,9}$=14.40 Hz, $J_{9,10}$=11.10 Hz	H8, 10
10	6.50, dd, $J_{9,10}$=11.10 Hz, $J_{10,11}$=13.32 Hz	H9, 11
11	7.41, dd, $J_{10,11}$=13.32 Hz, $J_{11,12}$=12.22 Hz	H10, 12
12	6.38, dd, $J_{11,12}$=12.22 Hz, $J_{12,13}$=11.86 Hz	H11, 13
13	6.00, d, $J_{12,13}$=11.86 Hz	H12

[a]Recorded in CD_2Cl_2 at 500 MHz. [b]Recorded in CD_2Cl_2 at 360 MHz.

H-22 peak showed NOE. This result reconfirms the facts that the double bond between C-12 and C-13 is Z and C-13 is connected to the pyrone moiety. In addition, when the H-6 peak was irradiated, H-4 and H-8 peaks showed NOE. This result verifies the connectivity between C-6 and C-8.

Our discovery that when citreoviridin was exposed to incandescent, fluorescent, or sun light for brief period of time, there was a significant amount of another isomer, isocitreoviridin, generates question of which isomer, citreoviridin, or isocitreoviridin, is the real inhibitor.[2] In a different account, we reported that citreoviridin is an inhibitor of ATP hydrolysis and ATP synthesis catalyzed by beef heart mitochondrial enzyme F1-ATPase, but isocitreoviridin has no effect on either activity of the enzyme.[7]

References

1. Hirata, Y.; Goto, T.; Sakabe, N. *Tetrahedron Lett.* **1964**, 1825.
2. Suh, H.; Wilcox, C. S. *J. Am. Chem. Soc.* **1988**, *110*, 470.
3. To isolate isocitreoviridin from the mixture of citreoviridin and isocitreoviridin, normal phase HPLC was used with 3.5% MeOH/CH_2Cl_2. CH_2Cl_2 was filtered through Al_2O_3 column before using.
4. Nagel, D. W.; Steyn, P. S.; Scott, D. B. *Phytochemistry* **1972**, *11*, 627.
5. ^1H NMR (500 MHz, CD_2Cl_2) (CH_2Cl_2, internal standard) δ 7.41 (dd, 1H, $J_{10,11}$=13.3 Hz, $J'_{11,12}$=12.2 Hz, H11), 6.50 (1H, $J_{10,11}$=13.3 Hz, $J'_{9,10}$=11.1 Hz, H10), 6.45 (1H, $J_{8,9}$=14.4 Hz, $J'_{9,10}$=11.1 Hz, H9), 6.38 (1H, $J_{12,13}$=11.9 Hz, $J'_{11,12}$=12.2 Hz, H12), 6.34 (1H, $J_{8,9}$=14.4 Hz, H8), 6.00 (d, 1H, $J_{12,13}$=11.9 Hz, H13), 5.86 (s, 1H, H6), 5.46 (s, 1H, H17), 3.93 (br s, 1H, H4), 3.82 (s, 3H, H23), 3.77 (q, 1H, J=6.3 Hz, H2), 1.96 (s, 3H, H22), 1.93 (br s, 3H, H21), 1.33 (s, 3H, H20), 1.16 (s, 3H, H19), 1.13 (d, 3H, J=6.3 Hz, H1).
6. Furusaki, A.; Watanabe, T.; Sakate, T.; Hirata, Y. 22nd Annual Meeting of the Chemical Society of Japan, Tokyo; 1969; Program of Abstracts #1626.
7. Saywood, S. F.; Suh, H.; Wilcox, C. S.; Schuster, S. M. *Arch. Biochem. Biophys.* **1989**, *270*(2), 714.

Unusual Rearrangement of 2-Amino-1-Substituted Phenyl-1-Alkanol to 1-Substituted phenyl-2-Alkanone

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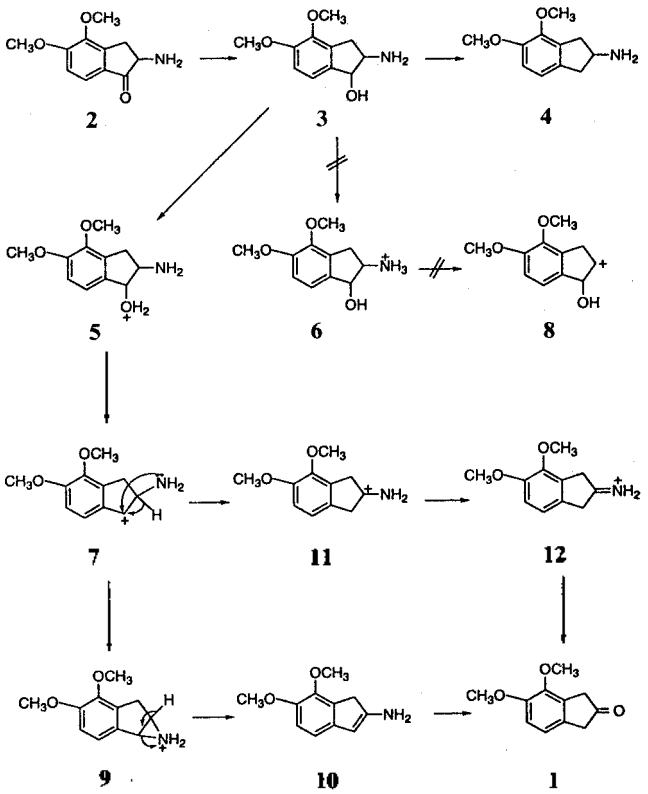
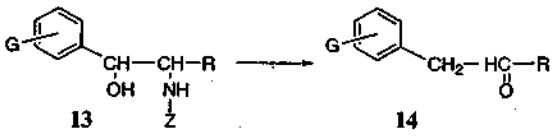
Illustrating the previously reported results,[1-3] in brief (scheme), the carbonyl group to the benzene ring of the aminoketone **2** was easily removed by the hydrogenolysis in the presence of 10% palladium on charcoa; the intermediate aminoalcohol, 2-amino-4,5-dimethoxy-1-indanol **3** was not isolated, but **3** was continously hydrogenated in the presence of $HClO_4$ in glacial acetic acid at 70 ℃ for 24 hours, to bring about hydrogenolysis of the benzylic hydroxyl group[4] directly to give 2-amino-4,5-dimethoxy-indane **4**. However, the catalytic reduction of **2** gave exclusively the desired reduction product **4** along with a small amount of a white solid, having a higher mobility than that of **4** on thin layer chromatogram. The white compound was thus believed to be a 4,5-dimethoxy-2-indanone **1** in view of the spectral characteristics (^1H and ^{13}C NMR, Mass, IR) and analytical data.[1,3]



Scheme 1. Plausible Mechanism for the Rearrangement Product Formation of Ketone **1** from the Aminoalcohol **3**.

Table 1. Rearranged Product Formation of Ketone **14** from the Aminoalcohol **13**



13 **14**

Comp. no	G	Z	R	Yield[a] (%)
13a	H	H	H	21
b	H	CH_3	H	18
c[b]	H	H	CH_3	35
d[c]	H	CH_3	CH_3	30
e[d]	3,4-$(OH)_2$	H	H	25
f	3,4-$(OH)_2$	CH_3	H	23
g	2-Cl	H	CH_3	43
h	4-Cl	H	CH_3	40
i	4-CH_3	H	CH_3	37
j	4-OCH_3	H	CH_3	47

[a]Chromatographed, silica gel in 20% $CHCl_3$ in hexane. [b]Norephedrine, [c]Ephedrine. [d]Noradrenaline. [e]Adrenaline.

The following scheme shows a plausible mechanism for the formation of the rearranged product **1** from **3**. A central problem in the fundamental understanding of a plausible mechanism at the amino alcohol intermediate stage **3**, is the question of whether the aminoalcohol **3** involves either kinetically controlled protonation at the hydroxyl oxygen to form oxnium ion **5** or thermodynamically controlled protonation at the basic nitrogen atom to form the ammonium salt **6** under the acidic conditions of the catalytic hydrogenation step. Since the good leaving groups are those that can best stabilize an extra pair of electrons, that is considered to be a weak base.[5] However, the stronger base, NH_3 is difficult to leave as a leaving group[6] as in **6**, and therefore the weaker base OH_2 will become a better leaving group, thus making oxonium ion **5** the sole reactive intermediate. Secondly, the generated carbonium ion **7** has relatively good deal of influences on the speed of this ionization which partly depends on the stability of the benzylic carbonium ion formed. The much more stable, long-lived benzylic carbonium ion **7** will predominantly favor the mechanistic routes **5**→**7**→**9**, excluding a route **6**→**8**.

With the above two controlling factors, the protonated oxonium ion **5** is preferentially formed and then converted to the enamine **10**[7] which was hydrolyzed to give the rearranged product **1** eventually. However, the pinacol-pinacolone type rearrangement from the hydride shift of **7** to **11**, followed by the immonium ion salt formation **12**, has not been eliminated as a possibility. On the basis of the presently available data, the enamine-favored mechanistic path is more compatible, and it is reasonable to discard the route of **6**→**8**.

In this work, we have studied the rearranged product formation of ketone **14** from the aminoalcohol **13** (Table).

The aminoalcohols **13a-o**[8] (0.0022 mol) were dissolved in glacial acetic acid (50 mL) and added $HClO_4$ (1 mL), and the reaction mixture was heated at 70 ℃ for 24 hours. On the end of the reaction the reaction mixture was cooled and treated with KOAc (1 g); $KClO_4$ precipitated immediately and was remmoved by filtration. The filtrate was taken up to dryness under reduced pressure, and $CHCl_3$ (50 mL) was added to the residue, which was washed with saturated $NaHCO_3$ solution (2×30 mL), NaCl solution (2×30 mL), and H_2O (2×30 mL). The $CHCl_3$ solution was dried ($MgSO_4$). Filtration and evaporation *in vaccuo* gave crude residue. The residue was chromatographed on silica gel eluted with 20% chloroform in hexane to give ketones **14 a-o**.[9]

This unusual rearrangement provides an one-step route to the synthesis of various kinds of aminoketones **14 a-o** from the benzylic aminoalcahals **13 a-o**. Extension of this kinds should be investigated further.

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References

1. Cannon, J. G.; Kim, J. C. J. *Med. Chem.* **1972**, *15*, 348.
2. Long, J. P.; Heintz, S.; Cannon, J. P.; Kim, J. C. *J. Pharmucol. Exp. Ther.* **1975**, *192*, 336.
3. Kim, J. C. *Bull. Chem. Soc. Jpn* **1981**, *54*, 3197. The compound, 4,5-dimethoxy-2-indanone 1 was fully characterized (^{1}H NHR and ^{13}C NMR, MP, Mass, IR), and showed satisfactory analytical data.
4. Sandler, S. R. Karo, W. *Organic Functional Group Preparations* I, II, III; Academic Press: New York, 1972.
5. March, J. *Advanced Organic Chemistry, Reaction, Mechanisims and Structure*, 3rd Ed.; John-Wiley and sons: 1985; pp 260-286.
6. The strong base such as NH_3 as a leaving group is seldom seen, except in the treatment of amino function with HNO_2.
7. Lowry, T. H.; Richardson, K. H. In *Mechanisim and Theory in Organic chemistry*, 2nd. Ed.; Harper and Row Publishing: 1981; pp 339-342.
8. The aminoalcohols, **13 g-j** were synthesized by literature methods and others were obtained from commercial suppliers and were used without further purification.
9. Ketone compounds obtained were fully characterzed (^{1}H and ^{13}C NHR, M.S., I.R and M.P.) and showed satisfactory microanalytical data.