

Table 1. Selected ^1H NMR Data for Isocitreoviridin

C #	δ $^1\text{H}^a$	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

^aRecorded in CD_2Cl_2 at 500 MHz. ^bRecorded 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

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

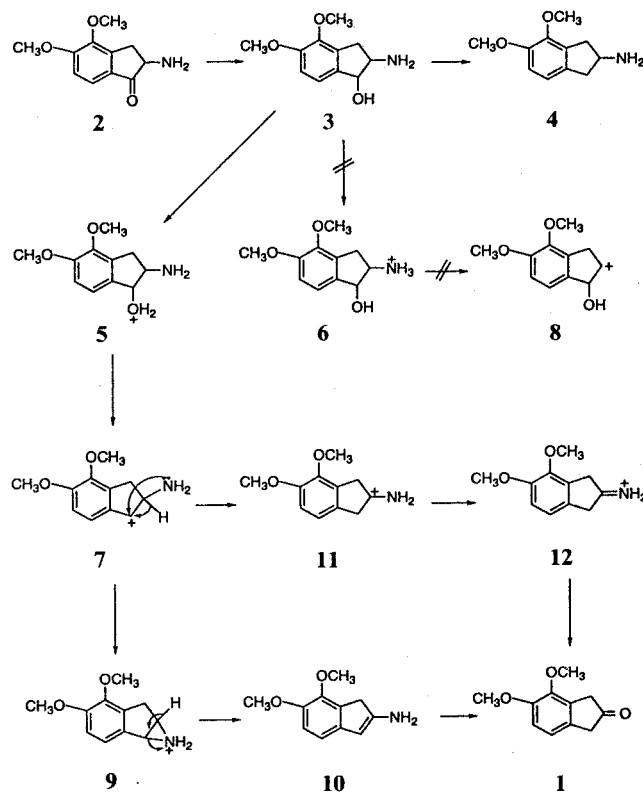
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Illustrating the previously reported results,¹⁻³ in brief (scheme), the carbonyl group to the benzene ring of the aminoketone **2** was easily removed by the hydrogenolysis in the presence of 10% palladium on charcoal; the intermediate aminoalcohol, 2-amino-4,5-dimethoxy-1-indanol **3** was not isolated, but **3** was continuously hydrogenated in the presence of HClO_4 in glacial acetic acid at 70°C for 24 hours, to bring about hydrogenolysis of the benzylic hydroxyl group⁴ 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**

$$\text{G}-\text{C}_6\text{H}_4-\text{CH}(\text{OH})-\text{CH}(\text{NHZ})-\text{R} \longrightarrow \text{G}-\text{C}_6\text{H}_4-\text{CH}_2-\text{C}(=\text{O})-\text{R}$$

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

^aChromatographed, silica gel in 20% CHCl₃ in hexane. ^bNorephedrine, ^cEphedrine. ^dNoradrenaline. ^eAdrenaline.

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 oxonium 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, NH₃ is difficult to leave as a leaving group⁶ as in **6**, and therefore the weaker base OH₂ 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 HClO₄ (1 mL), and the reaction mixture was heated at 70 °C for 24 hours. On the end of the reaction the reaction mixture was cooled and treated with KOAc (1 g); KClO₄ precipitated immediately and was removed by filtration. The filtrate was taken up to dryness under reduced pressure, and CHCl₃ (50 mL) was added to the residue, which was washed with saturated NaHCO₃ solution (2×30 mL), NaCl solution (2×30 mL), and H₂O (2×30 mL). The CHCl₃ solution was dried (MgSO₄). Filtration and evaporation *in vacuo* 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 aminoalcohols **13 a-o**. Extension of this kinds should be investigated further.

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References

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3. Kim, J. C. *Bull. Chem. Soc. Jpn* **1981**, *54*, 3197. The compound, 4,5-dimethoxy-2-indanone **1** was fully characterized (¹H NMR and ¹³C NMR, MP, Mass, IR), and showed satisfactory analytical data.
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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 characterized (¹H and ¹³C NMR, M.S., IR and M.P.) and showed satisfactory microanalytical data.