2-Bromo-2-cyano-N-methylacetamide——This compound was obtained from N-methylcyanoacetamide by the same method as described above for 2-bromo-2-cyanoacetamide, but less amount of AcOH–Ac_2O was used because of easier solubility of the substrate. Yield, 81%. Prisms (from EtOH), mp 93—97°. IR ν_{max}^{KBr} cm^{-1}: 2244 (CN), 1667 (CO). *Anal.* Calcd. for $C_4H_5ON_2Br$: C, 27.14; H, 2.85; N, 15.82; Br, 45.15. Found: C, 27.34; H, 3.17; N, 15.75; Br, 45.73.

2-Bromo-2-cyano-N,N-dimethylacetamide——This compound was obtained from N,N-dimethylcyanoacetamide by the same method as described for 2-bromo-2-cyanoacetamide, but less amount of AcOH–Ac_2O was used because of easier solubility of the substrate. Yield, 85%. Prisms (from ether), mp 53—54°, bp 134—135° (3 mmHg). IR ν_{max}^{KBr} cm^{-1}: 2260 (CN), 1665 (CO). NMR τ (in 10% $CDCl_3$): 4.82 (1H, s, CH), 6.81 and 6.93 (6H, 2s, $2CH_3$). *Anal.* Calcd. for $C_5H_7ON_2Br$: C, 31.44; H, 3.69; N, 14.65; Br, 41.98. Found: C, 30.99; H, 4.01; N, 14.68; Br, 41.83.

2-Amidino-2-bromoacetamide——Into a vigorously stirred suspension of 13.8 g (0.1 mole) of amidinoacetamide hydrochloride[6] in 120 ml of AcOH–Ac_2O mixture (10: 1 in volume) 16.0 g (0.1 mole) of bromine in 32 ml of AcOH was dropwise added at 8—10°. After stirring for additional 3 hr at room temperature, the homogeneous solution was concentrated under reduced pressure. The resulting oily residue was washed with dry ether and thoroughly triturated with dioxane until solidified. Recrystallization from EtOH–dioxane (1: 2) gave leaves, mp 132—133° (decomp.). Yield, 30.8 g (88%). This material was shown to be an equimolar addition compound of 2-amidino-2-bromoacetamide, hydrogen bromide and dioxane $\left(\begin{matrix}H_2N\\HN\end{matrix}\!\!>\!CCHBrCONH_2\cdot HBr\cdot C_4H_8O_2\right)$. *Anal.* Calcd. for $C_7H_{15}O_3N_3Br_2$: C, 24.09; H, 4.33; N, 12.04. Found: C, 24.25; H, 4.66; N, 12.12.

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Formation of Morphinandienone-type Compound through Methylenedioxy Cleavage by Pschorr Cyclization[1,2]

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Sinomenine (I), an alkaloid isolated from *Sinomenium acutum*, was assigned to the morphinanenone structure, and Barton and his co-workers[4] suggested that the biogenesis of sinomenine (I) would be performed from (+)-reticuline (II) to give α-diketone (IV) through sinoactine (III). The α-diketone (diosphenol) was a key intermediate in the biosynthesis of sinomenine.

We have reported a simple total synthesis of morphinandienone alkaloids, (±)-amurine (V),[5] (±)-flavinantine (VI),[6] salutaridine (VII),[7] and sinoactine (III).[7] Herein we wish to report a simple synthesis of a model α-diketone type compound (VIII) through cleavage

1) This forms Part DLVI of "Studies on the Syntheses of Heterocyclic Compounds," by T. Kametani.
2) This work was reported as a communication in *Chem. Ind.*, **1969**, 833.
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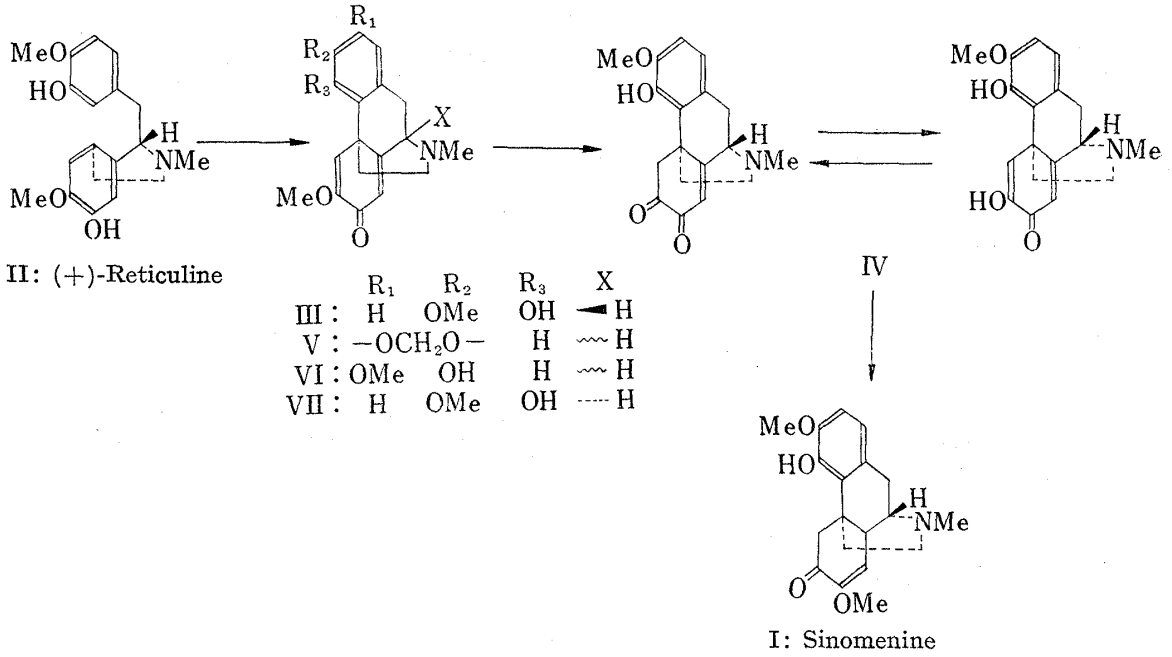

Chart 1

of the methylenedioxy group by a modified Pschorr reaction, which is similar to a key intermediate, α-diketone (IV) in the biosynthesis of sinomenine (I).

Diazotization of 1-(2-amino-4,5-dimethoxybenzyl)-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (X)[8] as usual, followed by decomposition of the resulting diazonium salt without metallic catalyst at 70° for 2 hr, was carried out to give four compounds as follows: the first compound obtained from chloroform eluant was assigned to the (±)-dicentrine (XI)[8] by its spectral data. Namely, the mass spectrometry showed the molecular ion at *m/e* 339 and its ultraviolet (UV) spectrum showed a typical aporphine absorption at 282 and 305.5 nm. Its assignment was also supported by its nuclear magnetic resonance (NMR) spectrum [τ in $CDCl_3$ 7.48 (NMe), 6.10 (2×OMe), 4.12 (1H, OCH_2O), 3.98 (1H, OCH_2O), 3.55 (C_3-H), 3.26 (C_8-H), 2.38 (C_{11}-H)].

The second compound obtained from chloroform eluant was rechromatographed on alumina to give a pale yellow syrup, whose structure was assigned an α-diketone compound (VIII) formed by the cleavage of the methylenedioxy group from the following spectral data. The high resolution mass spectrometry (M^+; *m/e* 327.161) also verified the molecular formula of $C_{19}H_{21}O_4N$ (Calcd. M^+; *m/e* 327.162). Infrared (IR) and UV spectra showed absorptions at 3400, 1652, 1626 cm^{-1} ($CHCl_3$) and that at 236 and 286 nm (methanol), respectively. Furthermore, the NMR spectrum (τ in $CDCl_3$) showed three methyl resonances at 7.55 (NMe), 6.17 (OMe), 6.13 (OMe), as singlets and two olefinic protons and two aromatic protons at 4.14, 3.63, 3.30, 3.21 as each singlet. These spectral data and thin-layer chromatography (TLC) value were also identical with those of the authentic α-diketone derivative (VIII).[9]

The third compound, which was eluted with chloroform–methanol (99:1, v/v), gave (±)-cassythicine[10] (XII), mp 116—122° (decomp.) (lit.,[11] mp 116—122°) which was recrystallized from methanol. IR spectrum ($CHCl_3$) showed an absorption at 3500 cm^{-1} and UV spectrum ($CHCl_3$) showed a typical aporphine system at 282 and 307 nm. Furthermore, the NMR spectrum (τ in $CDCl_3$) showed two methyl resonances at 7.45 (NMe) and 6.10 (OMe),

8) R.D. Haworth, W.H. Perkin, Jr., and J. Perkin, *J. Chem. Soc.*, **1925**, 2018.
9) T. Kametani, T. Sugahara, H. Yagi, K. Fukumoto, B.R. Pai, and R. Charubala, *J. Chem. Soc.* (*C*), **1970**, 624.
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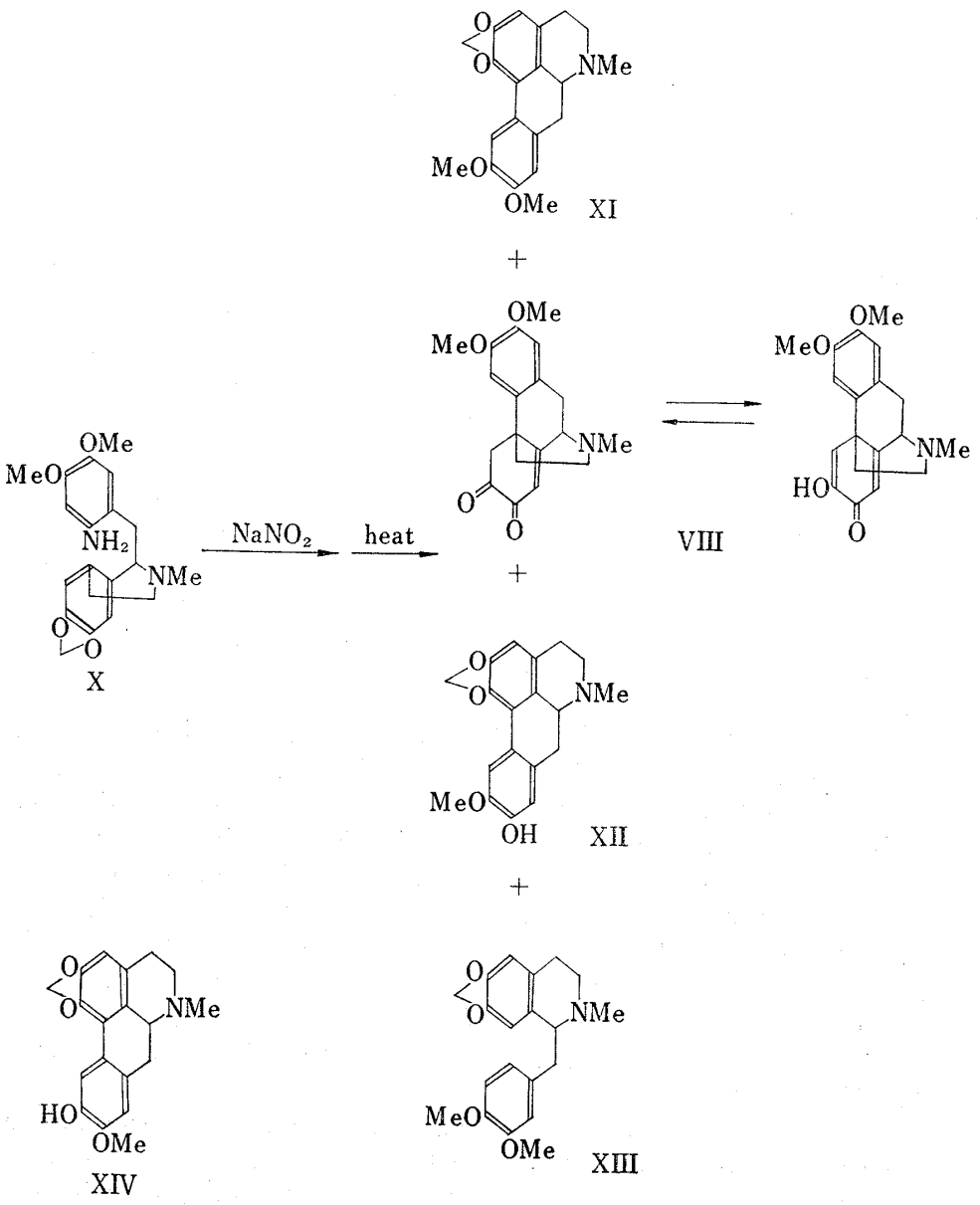

Chart 2

as singlet, methylene protons of methylenedioxy group at 3.93 (1H, J=1.7 Hz), 4.10 (1H, J=1.7 Hz) as doublet, and aromatic protons at 3.50 (C_3-H), 3.21 (C_8-H), and 2.38 (C_{11}-H). These results proved that the third product was not phanostenine (XIV).[12]

Finally, the deamination product, 1,2,3,4-tetrahydro-1-(3,4-dimethoxybenzyl)-2-methyl-6,7-methylenedioxyisoquinoline (XIII), which was eluted with chloroform–methanol (99:1, v/v), was obtained as the fourth compound, and the structural assignment was achieved by the following NMR spectral data [τ in $CDCl_3$ 7.54 (NMe), 6.23 (OMe), 6.19 (OMe), 4.20 (OCH_2O), and aromatic protons at 3.71 (1H), 3.50 (1H), 3.39 (1H), 3.30 (2H) as each singlet].

Experimental[13]

The Modified Pschorr Reaction of 1-(2-Amino-4,5-dimethoxybenzyl)-1,2,3,4-tetrahydro-6,7-methylenedioxyisoquinoline (X)——To a solution of 2.9 g of the aminoisoquinoline[8] (X) and 96 ml of 5% H_2SO_4 aq.

12) M. Tomita and I. Kikkawa, *Yakugaku Zasshi*, **77**, 1015 (1957).
13) All melting points are uncorrected.

solution was added dropwise 6.5 ml of 10% $NaNO_2$ aq. solution at 0—5° with stirring. After addition, the stirring was continued at the same temperature for 1 hr. Furthermore, the reaction mixture was heated gradually on a water bath to 70° and the stirring was continued at 70° for 2 hr. After heating, the cooled reaction mixture was basified with 10% aq. ammonia and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, and evaporated to give a brown reddish oil, which was chromatographed on 75 g of silica gel using $CHCl_3$ and MeOH as eluants.

Evaporation of the $CHCl_3$ (Fr. 3—6) gave 430 mg of a brown oil (XI), whose IR, UV, and NMR spectra were superimposable on those of the (±)-dicentrine.[8,14] UV λ_{max}^{MeOH}: 282, 305.5 nm; NMR (τ in $CDCl_3$): 7.48 (3H, singlet, NMe), 6.10 (6H, singlet, 2×OMe), 4.12 (1H, doublet, J=1.7 Hz, $OC\underline{H}_2O$), 3.98 (1H, doublet, J=1.7 Hz, $OC\underline{H}_2O$), 3.55 (1H, singlet, C_3-H), 3.26 (1H, singlet, C_8-H) and 2.38 (1H, singlet, C_{11}-H). Mass Spectrum m/e: M^+ 339.

The second $CHCl_3$ eluant (Fr. 7—10) gave 230 mg of a brown oil (VIII), which was again chromatographed on alumina using benzene and $CHCl_3$ as eluants. Evaporation of the benzene–$CHCl_3$ (1: 1) eluate gave 180 mg of a pale yellow syrup, which was assigned an α-diketone type compound formed by cleavage of the methylenedioxy group. Mass Spectrum: M^+ 327.161 (Calcd. M^+ 327.162, $C_{19}H_{21}O_4N$); NMR (τ in $CDCl_3$): 7.55 (3H, singlet, NMe), 6.17 (3H, singlet, OMe), 6.13 (3H, singlet, OMe), 4.14, 3.63, 3.30, 3.21 (4×1H, each singlet, C_1-H, C_4-H, C_5-H, C_8-H); IR $\nu_{max}^{CHCl_3}$: 3400 (OH), 1652 (C=O), 1626 (C=C) cm^{-1}; UV λ_{max}^{MeOH}: 236, 286 nm. These spectral data were superimposable on those of an authentic α-diketone derivative[9] (VIII).

The third $CHCl_3$–MeOH (99: 1) eluant (Fr. 12—13) gave 60 mg of a brown oil (XII), which was recrystallized from MeOH to give colorless prisms, mp 116—122°, identical with the authentic (±)-cassythicine.[10] UV λ_{max}^{MeOH}: 282 and 307 nm; IR $\nu_{max}^{CHCl_3}$ 3500 (OH) cm^{-1}; NMR (τ in $CDCl_3$): 7.45 (3H, singlet, NMe), 6.10 (3H, singlet, OMe), 3.93, 4.10 (2×1H, each doublet, J=1.7 Hz, $OC\underline{H}_2O$), 3.50 (1H, singlet, C_3-H), 3.21 (1H, singlet, C_8-H), 2.38 (1H, singlet, C_{11}-H).

Finally, removal of $CHCl_3$–MeOH (99: 1) eluant (Fr. 15) gave 10 mg of XIII as pale yellow oil, identical with the 1,2,3,4-tetrahydro-1-(3,4-dimethoxybenzyl)-2-methyl-6,7-methylenedioxyisoquinoline.[8,14] NMR (τ in $CDCl_3$): 7.54 (3H, singlet, NMe), 6.23 (3H, singlet, OMe), 6.19 (3H, singlet, OMe), 4.20 (2H, singlet, $OC\underline{H}_2O$), 3.71 (1H, singlet, Ar-H), 3.50 (1H, singlet, Ar-H), 3.39 (1H, singlet, Ar-H), 3.30 (2H, singlet, 2×Ar-H).

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14) T. Haginiwa and I. Murakoshi, *Yakugaku Zasshi*, **75**, 462 (1955).