After cooling, the solid obtained was recrystallized from AcOEt-petr. benzine to colorless platelets, m.p. 83.5—85°. This substance gave a negative permanganate test in acetone. Anal. Calcd. for 

\[ C_{11}H_{14}O_4 \]

C: 64.07; H: 4.89. Found: C, 63.61; H, 4.86.

3-(\(\alpha\)-Carboxyphenyl)butyric Acid (V)—A solution of 2 g. of (IIIa) in 60 cc. of 10\% NaOH was heated under stirring at 90° in a water bath. Raney Ni alloy was then added to the solution in small portions over a period of 90 mins. The solution was heated for additional 1 hr. After cooling, the precipitated Ni was filtered and washed with water. The combined aqueous layer was acidified with conc. HCl and the solid obtained formed white crystals from water, m.p. 147.5—149.5°. An admixture with the sample of \(\beta\)-(\(\alpha\)-carboxyphenyl)butyric acid, m.p. 148—150°, prepared by th ring-opening of 2-cyano-3-methyl-1-indanone, gave no depression of the melting point. The yield was 1.9 g. (95\%). Anal. Calcd. for 

\[ C_{11}H_{14}O_4 \]

C: 63.45; H: 5.81. Found: C, 63.27; H, 5.85.

### Summary

The Reformatsky reaction of ethyl \(\alpha\)-acetylbenzoate (II) with ethyl bromoacetate gave ethyl 3-methylphthalide-3-acetate (IIIa) as the product, which was led to 3-(\(\alpha\)-carboxyphenyl)butyric acid (I) via 3-(\(\alpha\)-carboxyphenyl)crotonic acid (IVa).

The structures of (IIIa) and (IVa) were established by means of their chemical properties and the ultraviolet and infrared absorption spectra, and it was shown that the method was valuable for the verification of each structure of the tautomerism represented by the following general formulae:

\[
\text{COOH} \quad \text{and} \quad \text{CO} \quad \text{CH}_2 \quad \text{COOR}'
\]

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(Pharmaceutical Institute, Medical Faculty, University of Kyoto)*

In view of the recent report concerning the isolation of N-methylisocorydine of the aporphine type from Fagara coco (Gill) Engr.\(^1\) and Xanthoxyllum spp.\(^2\) of the Rutaceae family, there seems to be a possibility that some of Rutaceous plants may yield other quaternary alkaloids besides those of the berberine type since so far only berberine type of alkaloids are known throughout the family.

Our attention was first directed to Phellodendron amurense Rupr. (Japanese name "Kihada") when it was noted that Murayama and Shinozaki,\(^3\) and Takada\(^4\) in an investigation of this plant reported only the presence of berberine-type alkaloids.

The methanol extract of the plant material, after removal of berberine-type alkaloids as the hydrochlorides, was treated by the modification of the previously reported procedure.\(^5\) After purification by reineckate precipitation there was isolated a basic substance as the picrate crystallizing in orange-yellow microscopic pillars, m.p. >300°. It gave analytical values corresponding to \(C_9H_9N_2\cdot C_3H_6O_3N_8\), and contains no methoxyl nor N-methyl group. The styrphate formed orange-yellow microscopic pillars, \(C_9H_9N_2\cdot C_3H_6O_3N_8\).

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m.p. > 230°. An aqueous solution of the hydrochloride caused no precipitate by Meyer's reagent, but it produced pink-colored precipitate with ammonium reineckate. With ninhydrin it gave no color, but an orange-red color with Dragendorff's reagent.5) The test for a guanidino group was positive. These experimental results exhibited a close similarity to guanidine, the identity of which was further confirmed by direct comparison of the infrared spectra of their respective picrates.

The second alkaloid was isolated as the styphnate, yellow needles, m.p. 230~231° (decomp.), from the mother-liquor of guanidine picrate, which was shown by infrared spectrum determination to be identical with magnoflorine.6)

The mother-liquor left after separation of magnoflorine styphnate was treated with aqueous potassium iodide, whereby the iodide was separated as a brownish oil, which upon crystallization from a mixture of ethanol, methanol, and acetone, formed colorless prisms, m.p. 259°. Analyses of the iodide were in accord with the formula C_{29}H_{43}O_{3}NI, [α]_{D}^{25} = -147° (methanol). Its infrared spectrum showed the presence of a phenolic hydroxyl function. It gave a negative test for a methylenedioxy group with Gaebel's and Labat's reagents. The ultraviolet absorption spectrum of the iodide is shown in Fig. 1.

![Fig. 1. Ultraviolet Absorption Spectrum of Phellodendrine Iodide (in MeOH soln.)](image)

The third alkaloid appears to be new and it is proposed to designate it phellodendrine. Because of the small amount available, however, a precise description of the basic skeleton of phellodendrine must await further experiments.

The residual substance from the mother-liquor of phellodendrine iodide was obtained as a crystalline styphnate forming yellow needles and decomposing around 230° with explosion. With ninhydrin it gave no color, but with Dragendorff's reagent it developed an orange-red color. With Meyer's reagent it produced no precipitate and analyses confirmed the absence of methoxyl and N-methyl groups. The test for sulfur and the Beilstein's test were negative. This substance appears to differ somewhat from guanidine in its properties, but its small amount did not permit further investigations.

The foregoing results are summarized below.

<table>
<thead>
<tr>
<th>Phellodendron amurense Rupr.</th>
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<tbody>
<tr>
<td>{ Berberine</td>
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<tr>
<td>Palmatine</td>
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<tr>
<td>Magnoeflorine</td>
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<tr>
<td>Phellodendrine (new alkaloid)</td>
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<tr>
<td>Guanidine</td>
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<tr>
<td>Unknown base</td>
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</tbody>
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We are indebted to Mr. S. Asano of Alps Pharmaceutical Co., Furukawa-cho, Gifu, for providing us with the plant material used in this work; to Mr. Narisada of the Research Laboratory, Shionogi & Co. Ltd., for measurement of the infrared spectra, and to Mr. Takashima of Osaka University for the ultraviolet absorption spectral data.

**Experimental**

*Isolation of the Alkaloids from Phellodendron amurense Rupr.*; Guanidine—Two kg. of the dried bark of the plant material was coarsely ground and extracted 3 times with boiling MeOH. The methanolic extract was evaporated in vacuo and the syrupy residue was diluted with a small amount of water and acidified by addition of conc. HCl. The crude berberine hydrochloride soon deposited, which was filtered and weighed 169 g. The filtrate was then treated with aq. ammonium reineckate, and the resulting precipitate was decomposed in acetone solution with aq. Ag$_2$SO$_4$ and then with aq. BaCl$_2$. The filtered solution now containing quaternary bases as the chlorides was concentrated in vacuo below 50° to a small volume and shaken up with ether to remove impurities. The aq. layer was evaporated in vacuo below 50° to dryness, the residue was dissolved in a minimum amount of water, and treated with aq. sodium picrate. The resulting precipitate was crystallized from acetone-MeOH to form orange-yellow, microscopic needles, m.p. >300°. Yield, 4.2 g. This picrate contains no methoxyl nor methylamino group. *Anal. Calcd.* for CH$_3$N$_2$·C$_6$H$_5$O$_3$N$_2$: C, 29.17; H, 2.80; N, 29.17. Found: C, 29.36; H, 2.95; N, 29.54.

A portion of the picrate was dissolved in a mixture of acetone and water, decomposed with 1% HCl, and the liberated picric acid was removed by means of ether. Evaporation of the aq. layer left a crystalline residue, which caused no precipitate with Meyer’s reagent but which gave pink-colored precipitate with aq. ammonium reineckate. It produced no color with ninhydrin, but a pink color with Dragendorff’s reagent. The test for a guanidyl group was positive.

The styrphate formed (from MeOH-EtOH) orange-yellow, microscopic pillars, m.p. >230°. *Anal. Calcd.* for CH$_3$N$_2$·C$_6$H$_5$O$_3$N$_2$: C, 27.64; H, 2.65; N, 27.63. Found: C, 27.77; H, 2.99; N, 27.81. This base was confirmed to be identical with guanidine by direct comparison of the infrared spectra of their respective picrates (Nujol mull).

**Magnoflorine**—The mother liquor from guanidine picrate was treated with 1% HCl and the liberated picric acid was eliminated by extraction with ether. The aq. layer was evaporated in vacuo below 50° to dryness, and the residue was dissolved in a minimum amount of water and treated with aq. sodium styrphate. The precipitate which formed was crystallized from acetone-MeOH to give 0.5 g. of yellow needles, m.p. 230–231°(decomp.). *Anal. Calcd.* for C$_8$H$_7$O$_3$N·C$_6$H$_5$O$_3$N$_2$: C, 53.24; H, 4.47. Found: C, 53.51; H, 4.71. This styrphate was found to be identical with magnoflorine styrphate by direct comparison of their infrared spectra (Nujol mull).

**Phellodendrine and Other Bases**—The mother liquor left after separation of magnoflorine styrphate was decomposed with HCl and the liberated styrphic acid was removed by ether. The aq. layer, after evaporation in vacuo below 50° to dryness, left a syrupy residue, which was dissolved in a minimum amount of water and treated with conc. aq. KI. The resulting oily precipitate was induced to crystallize from MeOH-EtOH-acetone, whereupon 30 mg. of colorless prisms, m.p. 259°, was obtained. $[\alpha]$_D$ = -147°$ ($c = 0.0816$, $l = 0.5$ dm. in MeOH). *Anal. Calcd.* for C$_{18}$H$_{14}$O$_7$N$_3$: C, 51.18; H, 5.15; N, 2.98. Found: C, 51.58; 51.60; H, 5.39; 5.51; N, 3.07; 3.19. This iodide gave a negative test for a methylenedioxy group with Gaebel’s reagent, and the infrared spectrum showed the presence of a phenolic hydroxyl function (Nujol mull). The ultraviolet absorption spectrum (MeOH solution) is shown in Fig. 1: $\lambda_{max}$ 287 m.$\mu$ ($log e$ 4.03).

The mother liquor separated from phellodendrine iodide by decantation was treated with aq. sodium styrphate, yielding yellow precipitate. It was crystallized from acetone-EtOH-MeOH to give 0.1 g. of yellow needles decomposing around 230° with explosion. This substance produced no precipitate with Meyer’s reagent but an orange-red color with Dragendorff’s reagent. It contains no methoxyl nor methylamino group. It also gave no color with ninhydrin. The test for sulfur and the Bielstein’s test were negative. The properties of this substance differs somewhat from guanidine styrphate, but because of its small amount no further investigation was made.

**Summary**

From the bark of *Phellodendron amurense* Rupr. (Rutaceae), four other quaternary alkaloids, guanidine, magnoflorine, phellodendrine (a new base), and an unknown base were isolated, besides those of the berberine type such as berberine and palmate.

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8) All melting points are uncorrected. We are indebted to Dr. K. Hozumi and the members of the Microanalytical Laboratory of this Institute for the microanalytical data.