acetate (V), mp 205—205.5° (IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1772(aromatic OAc), 1747 (aliphatic OAc), 1678 (quinone). NMR ($CDCl_3$) τ: 8.41 (3H, d, J=7 Hz, AcO–$\dot{C}$H–$\underline{CH}_3$), 7.38, 7.44, 7.58, 7.91 (each 3H, s, $OCOCH_3$), 3.98 (1H, q, J=7 Hz, AcO–$\dot{C}\underline{H}$–CH_3). Mass Spectrum m/e: 518(M^+)). The tetraacetate (V) was hydrolyzed with potassium hydroxide in aqueous methanol and subsequently methylated with dimethyl sulfate to give the trimethyl ether (VI), mp 91—94° (IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3470(OH), 1670(quinone). NMR ($CDCl_3$) τ: 8.40 (3H, d, J=7 Hz, HO–$\dot{C}$H–$\underline{CH}_3$), 5.97, 5.91, 5.86 (each 3H, s, OCH_3), 4.84 (1H, q, J=7 Hz, HO–$\dot{C}\underline{H}$–CH_3). Mass Spectrum m/e: 392(M^+)).

Ball oxidation of VI with manganese dioxide in benzene yielded the ketone (VII), mp 224—226° (IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1680(aromatic ketone), 1674, 1660(quinone). NMR ($CDCl_3$) τ: 7.22 (3H, s, $COCH_3$), 5.95 (6H), 5.80 (3H) (each s, OCH_3). Mass Spectrum m/e: 390(M^+)), which was identical with bisanhydrodaunomycinone dimethyl ether in mp, mixed mp, thin-layer chromatography, infrared(KBr) and mass spectra.

Demethylation of VII with ten molar equivalents of boron tribromide in methylene chloride at −60° gave selectively 8-acetyl-6,11-dihydroxy-1-methoxynaphthacenequinone (II), mp 320—325° (IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1683(aromatic ketone), 1615, 1605(chelated quinone). NMR (CF_3COOD) τ: 7.11 (3H, s, $COCH_3$), 5.98 (3H, s, OCH_3). Mass Spectrum m/e: 362(M^+)), which was identical with bisanhydrodaunomycinone in mp, mixed mp, thin-layer chromatography, infrared(KBr) and mass spectra.

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Isolation of 2,2,6,6-Tetramethylpiperidone-(4) from Pronase Lysate of Ox Brain as a Hypotensive Principle

Martini and his coworkers reported that acetone extracts obtained from brains of different animals show depressor activities on the mean arterial blood pressure of cat or guinea pig.[1–3)]

Later, the same workers indicated that an extract obtained from tryptic or chymotryptic lysate of brains possesses a clearly hypertensive effect, whereas that from papain lysate retains a hypotensive effect[4)], and they assumed that a certain substance showed hypertensive effect in reduced state and hypotensive effect in oxidized state and it might be interconvertible under

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1) E. Martini, A. Marzorati, and E. Morpurgo, *Experientia*, **8**, 225 (1952).
2) F. Chiesa, *Ist. Lombardo* (*Rend. Sc.*), **93**, 7 (1959).
3) F. Chiesa, *Ist. Lombardo* (*Rend. Sc.*), **93**, 26 (1959).
4) E. Martini, F. Chiesa, A. Spiga, and R. Oberosler, *Enzymologia*, **29**, 1 (1965).

physiological conditions.[5,6]

However, the chemical structures of these physiologically interesting substances remained undefined yet.

The present communication reports the isolation of 2,2,6,6-tetramethylpiperidone-(4) as a hypotensive principle from pronase lysate of ox brain.

The isolation of hypotensive substance was carried out as follows: Ox brain homogenate was incubated with pronase in phosphate buffer (pH 7.5) at 37° for 48 hr. The lysate was concentrated and extracted with chloroform–methanol (2: 1).

An active fraction obtained with the use of solvent extractions was subjected to a silicic acid chromatography, and the hypotensive activity was focused on an eluate with chloroform–methanol (95: 5), then it was chromatographed on Amberlite CG 50.

Finally, the hypotensive principle was crystallized from ethanol and acetone as hydrochloride, and it showed a single spot on thin-layer chromatography (TLC).

This hypotensive principle melts at 195° with decomposition and is analyzed for $C_9H_{17}NO \cdot HCl$.

An intravenous injection of this compound produces a fall of arterial blood pressure on anesthetized cat.

The structure of this hypotensive compound was determined to be 2,2,6,6-tetramethylpiperidone-(4) from infrared (IR) and nuclear magnetic resonance (NMR) and mass spectral data (*m/e*: 155, (M^+)). IR and NMR spectral data are shown in Fig. 1 and 2.

Furthermore, its structure was confirmed by synthesis after Francis' method from acetone and ammonia in the presence of calcium chloride[7], and homogenity was established by TLC on silica gel plates: *Rf* 0.48(methanol), *Rf* 0.50 (*n*-butanol–acetic acid–water, 4: 1: 2), *Rf* 0.51 (benzene–isopropanol–acetone–ammonia, 20: 35: 5: 1), and *Rf* 0.64 (80% phenol). Iodine vapour, premanganate, phosphomolybdate, and 2,4-dinitrpohenylhydrazine reagents served as detecting reagents.

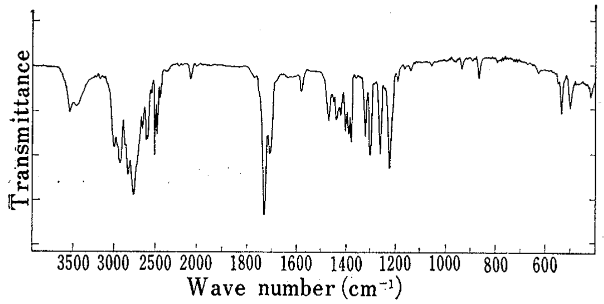

Fig. 1. IR Spectrum of Depressor Active Principle

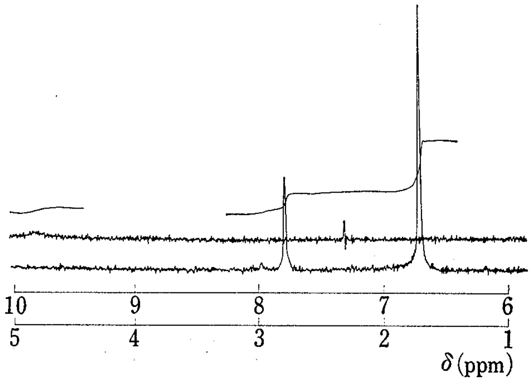

Fig. 2. NMR Spectrum of Depressor Active Principle

In an examination with papain, this hypotensive principle was also found in its hydrolysate.

It can be clearly distinguished from another hypotensive principle obtained from acetone extract of ox brain, and named as "D–I" by us.[8]

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5) F. Chiesa, E. Martini, R. Oberosler, and A. Spiga, *Enzymologia*, **29**, 38 (1965).

6) E. Martini, F. Chiesa, R. Oberosler, G. Maffeo, C. Secchi, *Enzymologia*, **33**, 100 (1967).

7) F. Francis, *J. Chem. Soc.*, 2867 (1927).

8) H. Tsukatani, T. Itami, T. Miyamoto, and T. Awazi, *Yakugaka Zasshi*, in press.

At present stage, it is difficult to solve whether this hypotensive substance is an artifact or not. However, it is probable that ammonia and some intermediates which belong to fatty acid degradation process are responsible for its formation.

Details of isolation, chemical properties, determination of chemical structure, synthesis and pharmacological activity of this compound will be reported later.

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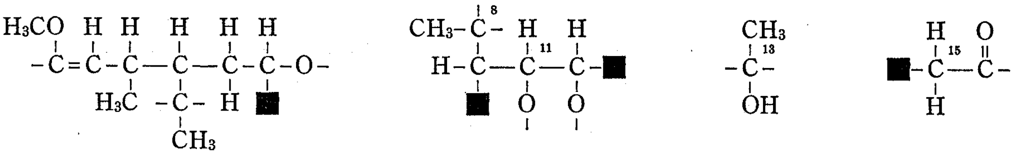
Stereostructure of Picrasin F, Simaroubolide of *Picrasma quassioides*

The Chemistry of the bitter principles of the quassia tree, *Picrasma quassioides* BENNETT (=*P. ailanthoides* PLANCHON) (Simaroubaceae) has made rapid advances during the past few years.[1–8] We have recently isolated another new bitter which is now designated as picrasin F. In this communication, evidence to propose formula I for picrasin F is described.

Picrasin F, mp 282—283°, has the molecular formula $C_{22}H_{30}O_8$ (M^+ at m/e 422 in mass spectrum). Of the eight oxygen atoms, one is involved in an α,β-disubstituted, α,β-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 262 nm, ν_{max} 1709, 1630 cm^{-1}, δ 5.21 ppm, $[\theta]_{340}$ −950), two in a δ-lactone (ν_{max} 1720 cm^{-1}, δ 4.67 ppm), one in a methoxyl (δ 3.48 ppm) and two in a methylene dioxy ring (δ 5.18, 5.37 ppm (J=1 Hz)). Since picrasin F shows infrared (IR) absorption for hydroxyls (ν_{max} 3475 cm^{-1}) but exhibits no NMR signal for a carbinyl hydrogen, the remaining two oxygens may be present as tertiary hydroxyls. Picrasin F also contains a secondary methyl (δ 0.89 ppm) and three tertiary methyls (δ 1.50, 1.54, 1.62 ppm) other than the methoxyl. Further analysis of the nuclear magnetic resonance (NMR) spectrum with the aid of double resonance experiments has demonstrated the presence of the following partial structures. Inter alia, intramolecular nuclear Overhauser effects were found between the C-11 hydrogen and the C-8 methyl hydrogens and between one of the C-15 hydrogens and the C-13 methyl hydrogens.



$$-\overset{H_3CO}{C}=\overset{H}{C}-\underset{H_3C}{\overset{H}{C}}-\underset{\underset{CH_3}{-C-}}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{■}{\overset{H}{C}}-O- \qquad H-\underset{■}{\overset{CH_3-\overset{8}{C}-}{C}}-\underset{O}{\overset{H}{\overset{11}{C}}}-\underset{O}{\overset{H}{C}}-■ \qquad -\underset{OH}{\overset{CH_3}{\overset{13}{C}}}- \qquad ■-\underset{H}{\overset{H}{\overset{15}{C}}}-\overset{O}{\overset{\|}{C}}-$$

■ : denotes a quaternary carbon

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1) T. Murae, T. Tsuyuki, T. Nishihama, S. Masuda, and T. Takahashi, *Tetrahedron Letters*, **1969**, 3013.
2) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 219 (1970).
3) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Bull. Chem. Soc. Japan*, **43**, 969 (1970).
4) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1082 (1970).
5) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Bull. Chem. Soc. Japan*, **43**, 3021 (1970).
6) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Chem. Pharm. Bull.* (Tokyo), **18**, 2590 (1970).
7) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 212 (1971).
8) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **99**, 2211 (1971).