CD, $[\theta]$ +676 (285 mμ), showing the 17–side chain to be β–oriented. As the cleavage of 14α,15α–epoxide with acid generally gives rise to 14β,15α–glycol,[11-15] the structure IX was assigned to the tetrahydroxy–ketone.

Oxidation of IX with Kiliani's reagnet gave a hydroxytetraketone, mp 262—266°, $C_{21}H_{28}O_5$, $[\alpha]_D^{23}$ +104.3±6.1° (c=0.235, $CHCl_3$). The IR spectrum in chloroform shows absorptions at 3281 (14β–OH), 1747 (15–ketone), 1707 (3– and 12–ketone) and 1697 cm^{-1} (20–ketone). Inspection of the IR spectrum in detail showed the presence of a strong hydrogen bonding between 14β–hydroxyl group (3281 cm^{-1}) and 20–carbonyl group (1697 cm^{-1}), giving further evidence that 17–side chain has the β–configuration. This product having 12–ketone and 17β–methyl ketone grouping proved to be identical with the hydroxy–tetraketone (IV) derived from purprogenin by mixed melting point and comparisons of TLC and IR spectra. These results established the structure of purprogenin to be 3β,14,15α–trihydroxy–14β,17β–pregn–5–ene–12,20–dione (I) as previously proposed by our group.

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A Novel Rearrangement of a Quinol Acetate[1]

Quinol acetates[2] prepared by the reaction of phenols with $Pb(OAc)_4$ are known to be rearranged to hydroquinones[3] under conditions of the Thiele reaction (Ac_2O–concd. H_2SO_4). We attempted to apply this method to tetrahydroisoquinolines in order to introduce hydroxyl group to benzene ring and chose corypalline (I) as a starting material.

Unexpectedly, we encountered a novel rearrangement, in which acetoxyl group moved to 4–position instead of 5–position (normal rearrangement).

A solution of I (200 mg, *ca.* 1 mmole) and $Pb(OAc)_4$ (680 mg, *ca.* 1.5 mmole) was stirred for 1.5 hour at room temperature, treated with ice–water, basified with $NaHCO_3$, and extracted with $CHCl_3$. Chromatography of the $CHCl_3$ layer on neutral Al_2O_3 (Woelm, elution with $CHCl_3$) gave N–methyl–10–acetoxy–6–methoxy–7–oxo–$\Delta^{5,6,8,9}$–hexahydroisoquinoline (II), mp 118—120° from *n*–hexane, (72 mg, 20%) [*Anal.* Calcd. for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.34; H, 6.94; N, 5.63. NMR τ: 7.92 (S., OAc), 7.61 (S., =NMe), 7.06, 6.68 (each d., C–1 *gem.* protons, J=12 cps), 6.34 (S., OMe), 4.20 (S., a vinylic proton), 3.82 (d., a vinylic proton, J=1.5 cps). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 (OAc), 1675, 1655, 1630 (dienone)].

A mixture of quinol acetate (II)(275 mg, *ca.* 1.1 mmole) in Ac_2O (4 ml) and concd. H_2SO_4 (0.3 ml) in Ac_2O (1 ml) was stood for 2 hours at room temperature. After adding crushed ice to the reaction mixture and extracting excess Ac_2O with ether, H_2O layer was

1) All melting points were uncorrected using Yanagimoto micro melting points measuring apparatus. All NMR spectra were measured at 60 Mc by JNR–C60S spectrometer in $CDCl_3$ using Me_4Si as internal standard. Gas–liquid chromatography (GLC) was taken with Shimadzu GC–1C gas chromatograph equipped with a hydrogen flame ionization detector.

2) F. Wessely and F. Sinwel, *Monatsh.*, **81**, 1055 (1950); J. D. London, "Progress in Organic Chemistry," Vol. 5, ed. by J. W. Cook and W. Carruthers, Butterworth & Co. (Publisher), Ltd., 1961, p. 51.

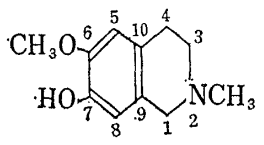
3) S. Goodwin and B. Witkop, *J. Am. Chem. Soc.*, **79**, 179 (1957).

basified with $NaHCO_3$, and a product was taken up with ether. This ether extract was chromatographed over silicic acid (Mallinckrodt) to furnish diacetate (III), elution with $CHCl_3$–MeOH (100:1), mp 82—84°(*n*-hexane), 140 mg (46.7% yield)[*Anal.* Calcd. for $C_{15}H_{19}O_5N$: C, 61.42; H, 6.53; N, 4.78. Found: C, 62.28, 62.07; H, 6.61, 6.76; N, 4.68, 4.81. NMR τ: 7.87, 7.70 (each s., two OAc), 7.54 (s., =NMe), 7.25, 7.10 (each d., ArCH(OAc)–C$\underline{H}_2$–N=, J=3.5 cps and J=3.0 cps), 6.72, 6.18 (each d., ArC$\underline{H}_2$–N(CH_3), J=15 cps), 6.17 (s., OMe), 4.00 (defused t., ArC$\underline{H}$(OAc)–CH_2–), 3.17,3.01 (each s., two aromatic protons). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1730 (OAc), 1620 (C=C)]; methiodide, mp 162—165° (decomp.) from *iso*-PrOH (*Anal.* Calcd. for $C_{16}H_{22}O_5NI \cdot 1\frac{1}{2}H_2O$: C, 41.56; H, 5.41; N, 3.03. Found: C, 41.19, 41.52; H, 5.20, 5.52; N, 2.73, 2.97).

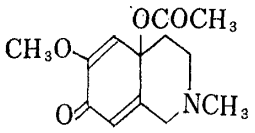
Structure of III was shown to be assigned as N-methyl-4,7-diacetoxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline by the above spectral data and by the fact that catalytic hydrogenolysis (10% Pd-C, AcOH, concd. H_2SO_4) of III yielded I.

Hydrolysis of III with 5% aq. KOH at room temperature gave 4,7-dihydroxy compound (IV), mp 153—155°(decomp.) from $CHCl_3$–*n*-hexane (*Anal.* Calcd. for $C_{11}H_{15}O_3N$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.17; H, 7.31; N, 6.50) and re-acetylation of IV (Ac_2O, pyridine) afforded III. This result indicated clearly the fact that no structural change occurred during hydrolysis.

Methylation of IV (CH_2N_2, MeOH) gave N-methyl-6,7-dimethoxy-4-hydroxy-1,2,3,4-tetrahydroisoquinoline (V), mp 127—128° (ϕH–*n*-hexane), [*Anal.* Calcd. for $C_{12}H_{17}O_3N$: C, 64.55; H, 7.68; N, 6.27. Found: C, 64.30; H, 7.83; N, 5.96. NMR τ: 7.63 (s., =NMe), 7.44, 7.12 (each d., ArCH(OH)–C$\underline{H}_2$–, J=3 cps), 6.92, 6.53 (each d., ArC$\underline{H}_2$–N(CH_3)–, J=15 cps), 6.11, 6.09 (each s., two OMe), 5.47 (defused t., ArC$\underline{H}$(OH)CH_2–), 3.54, 3.04 (each s., two aromatic protons). IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1605 (C=C)].

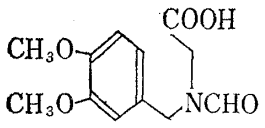


I

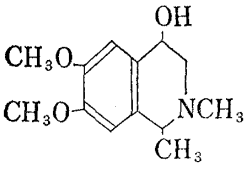


II

III : R=R_1=$COCH_3$
IV : R=R_1=H
V : R=CH_3, R_1=H



VI



VII

To prove the structure of V by an alternate synthesis and to search for modified tetrahydroisoquinoline synthesis (Pomeranz–Fritsch reaction), N-formyl-N-veratrylglycine (VI), from veratraldehyde and ethyl glycinate·HCl (four steps), mp 199—201°(MeOH)(*Anal.* Calcd. for $C_{12}H_{15}O_5N$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.91; H, 5.94; N, 5.45) was prepared.

Heating (70—75°) of VI in PPA[4] with stirring and chromatography of the product on Al_2O_3 (Merck) gave two kinds of compounds. The first (elution with ϕH) was unknown

4) *cf.* R.M. Carlson and R.K. Hill, *J. Org. Chem.*, **31**, 2385 (1966).

yellow crystals, mp 265°(decomp.)(ϕH) and the second [elution with ϕH–$CHCl_3$ (50:1–2:5)] was an oil [IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1690 (shoulder, α,β–unsaturated ketone), 1670 (=NCHO), 1600 (C=C)] respectively in 1:3 ratio. Refluxing of the oil with $LiAlH_4$ in ab. ether–ab. tetrahydrofuran for 4 hours and chromatography on silicic acid [elution with $CHCl_3$–MeOH(100:1–100:2)] afforded 4–hydroxy compound (*ca.* 12% yield), mp 124—126° from ϕH–*n*–hexane.

Identity of the 4–hydroxy compound and V from I was shown by comparison of their IR spectra ($CHCl_3$) and GLC (5% SE–30, 175°) and by mixed mp determination.

Thus V was undoubtedly 4–hydroxy compound and also tetrahydroisoquinolines could be prepared from glycine derivatives though in low yield.

Mechanistic details of the unusual rearrangement described above and synthesis of *dl*–gigantine (VII)[5] from *dl*–N–methylisosalsoline as an application of this method will be published in the near future.

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5) *d*–Gigantine [mp 151—152°, $[\alpha]_D$ 27.1°($CHCl_3$)] is isolated from *Carnegia gigantea* and the planar structure is assigned as VII. (J.E. Hodgkins, S.D. Brown, and J.L. Massingill, *Tetrahedron Letters*, **1967**, 1321).

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A Convenient Method for the Preparation of *tert*-Butyl Azidoformate

Progress in the peptide chemistry is accumulating data indicating the usefulness of the *tert*–butoxycarbonyl group (*t*–BOC) as a reversible protecting group for the amino function of amino acids and peptides, because of the ease of removal by mild acidolysis.[1,2] For the synthesis of complex peptides, such an acid labile protecting group is essential in addition to the historical benzyloxycarbonyl group.

Introduction of *t*–BOC group into amino acids requires multiple steps of reaction due to the unstability of *tert*–butyl chloroformate. For example, *t*–BOC amino acids are prepared by the reaction of the corresponding isocyanate with *tert*–butanol,[3] or by *tert*–butyl *p*–nitrophenyl carbonate[4] or *tert*–butyl cyanoformate[5,6] or *tert*–butyl azidoformate.[7–9] These pro-

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