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12. **Michitoshi Ohta and Lara Ohmori** : Studies on Abietic Acid Derivatives. I. Deisopropylation of Dehydroabietic Acid. (1).

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Parham and others$^{1)}$ had recently reported that boiling of dehydroabietic acid (Ia) in benzene, in the presence of aluminum chloride, had afforded a mixture of a small amount of crystals of m.p. 160° and of m.p. 138~140°, and assumed from their analytical values and absorption spectra that the former would be the deisopropylation product of (Ia), but failed to give any definite conclusion about its structure.

The present writers had been examining the method for deisopropylation of (Ia), as part of studies on the synthesis of azaditerpenoids, that the experiment of Parham and others was followed. It was thereby learned that the products are two steric isomers of m.p. 173° and of m.p. 162°, and that the former is a deisopropylated compound having the same steric configuration as that of (Ia), while the latter is also the same compound with the methyl at 12-position, between the fused rings, undergoing rearrangement to the α-configuration. Hereafter, therefore, the former compound of m.p. 173° will be designated as deisopropyldehydroabietic acid and the latter compound of m.p. 162° as deisopropylallodehydroabietic acid. Structural determination of these compounds will be described in this and the following papers.

On stirring (Ia) in dehydrated benzene with aluminum chloride and low-pressure distillation of the product affords a mixture melting at 136~140°. Treatment of this mixture with diisoamylamine with isopropyl ether as the solvent results in the precipitation of a salt melting at 150°, whose treatment with acetic acid gives an acid (IIb) of m.p. 160~162°. The mother liquor left after the removal of the salt is treated with acetic acid and affords another acid (IIa) of m.p. 171~173°. The yield from (Ia) is 6% of (IIa) and 44% of (IIb) but it is assumed from the specific rotation of the mixture of m.p. 136~140° and of each component, that these acids are formed in the ratio of (IIa) : (IIb) = 3 : 7.

The analytical values of (IIa) and (IIb) both agree with deisopropylated product of (Ia) and their methyl esters melt respectively at 108~109° (IIIa) and 93~94° (IIIb). Ultraviolet spectra of both (IIIa) and (IIIb) exhibit absorption maxima at 265 and 273 mμ, the bands having shifted 3 mμ to the shorter wave length compared to those in methyl dehydroabietate (Ib). Compared to M_D +186 for (Ia), those of (IIa) and (IIb) were respectively +179 and +4, suggesting (IIa) to retain the same steric configuration as that of (Ia).

One of the writers (Ohta) had earlier synthesized methyl 7-aminodeisopropyldehydroabietate (VII)$^{2)}$ and this compound was now diazotized by the usual method and reduced

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1) W.E. Parham, *et al.* : J. Am. Chem. Soc., **77**, 1166(1955).

2) M. Ohta : This Bulletin, **4**, 273(1956).

with alkaline formaldehyde solution. As anticipated, a deaminated compound of m.p. 108° was obtained and this was found by admixture to be identical with (IIIa).

Selenium dehydrogenation of (IIb) affords 1-methylphenanthrene (VIII) in a good yield that (IIb) is assumed to be an isomer of (IIa) in connection with the asymmetric carbon atoms at 11- and 12(or 1)-positions.

Oxidation of (IIIa) in acetic acid with chromium trioxide gives three kinds of a product. One is a ketone (IVa) of m.p. 53°, whose molecular rotation is close to that (+21)[3] of methyl 9-oxodehydroabietate (Ic). Since the ultraviolet spectra (cf. Fig. 1) of both showed similar absorptions, it seems certain that (IVa) is methyl 9-oxodeisopropyldehydroabietate.

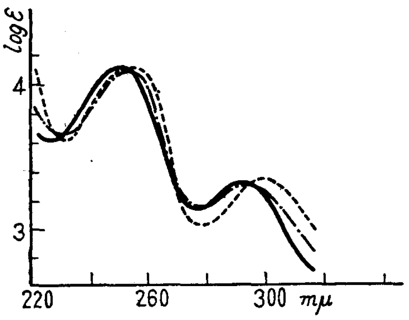

Fig. 1.

The second product occurs as yellow crystals (VIa) of m.p. 201~203°(decomp.), its analytical values agree with the formula $C_{18}H_{20}O_5$, and its ultraviolet spectrum (cf. Fig. 2) exhibits absorption maxima at 285 and 445 mμ. From these and the fact that its infrared spectrum shows absorptions at 3.01 (OH), 5.76 (ester), and 5.94 μ (conjugated ketone), it is assumed that (VIa) is 9,10-dioxo-11-hydroxy compound but no detailed examination has yet been made.

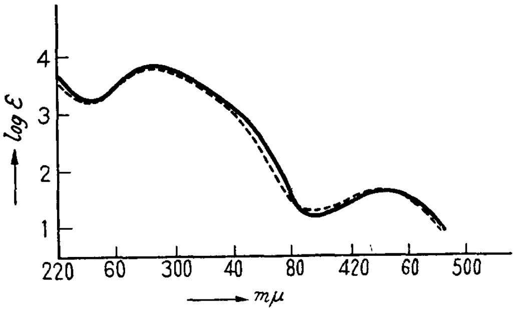

Fig. 2.

The third product is an acid (Va) of m.p. 151~152° and the compound is certain to be 2,6-dimethyl-2-(*o*-carboxyphenyl)-6-methoxycarbonyl-1-cyclohexanone from the values of carbon, hydrogen, and methoxyl determinations, neutralization equivalent, and ultraviolet spectrum (λ_{max} 285 mμ). As a reaction similar to this, Zeiss and others[4] carried out the oxidation of (Ib) with chromium trioxide, followed by heating the acid product to 120~160°, and obtained 2,6-dimethyl-2-(*o*-carboxy-*p*-isopropylphenyl)-1-cyclohexanone (IX), m.p. 154~156°, $[\alpha]_D$ +163°.

When 2.7 moles of chromium trioxide is used for (IIIa), the chief product is (IVa) in 60% yield, with about 1% of (Va) and about 10% of (VIa), but when 6.8 moles of chromium trioxide is used, (Va) is mainly formed, the yield reaching 65%.

Similar oxidation of (IIIb) with chromium trioxide in acetic acid affords an acid (Vb) of m.p. 128~131.5° and crystals (VIb) of m.p. 135~138°. The analytical values of (Vb) agree with those of (Va) and since its ultraviolet spectrum exhibits absorption maximum

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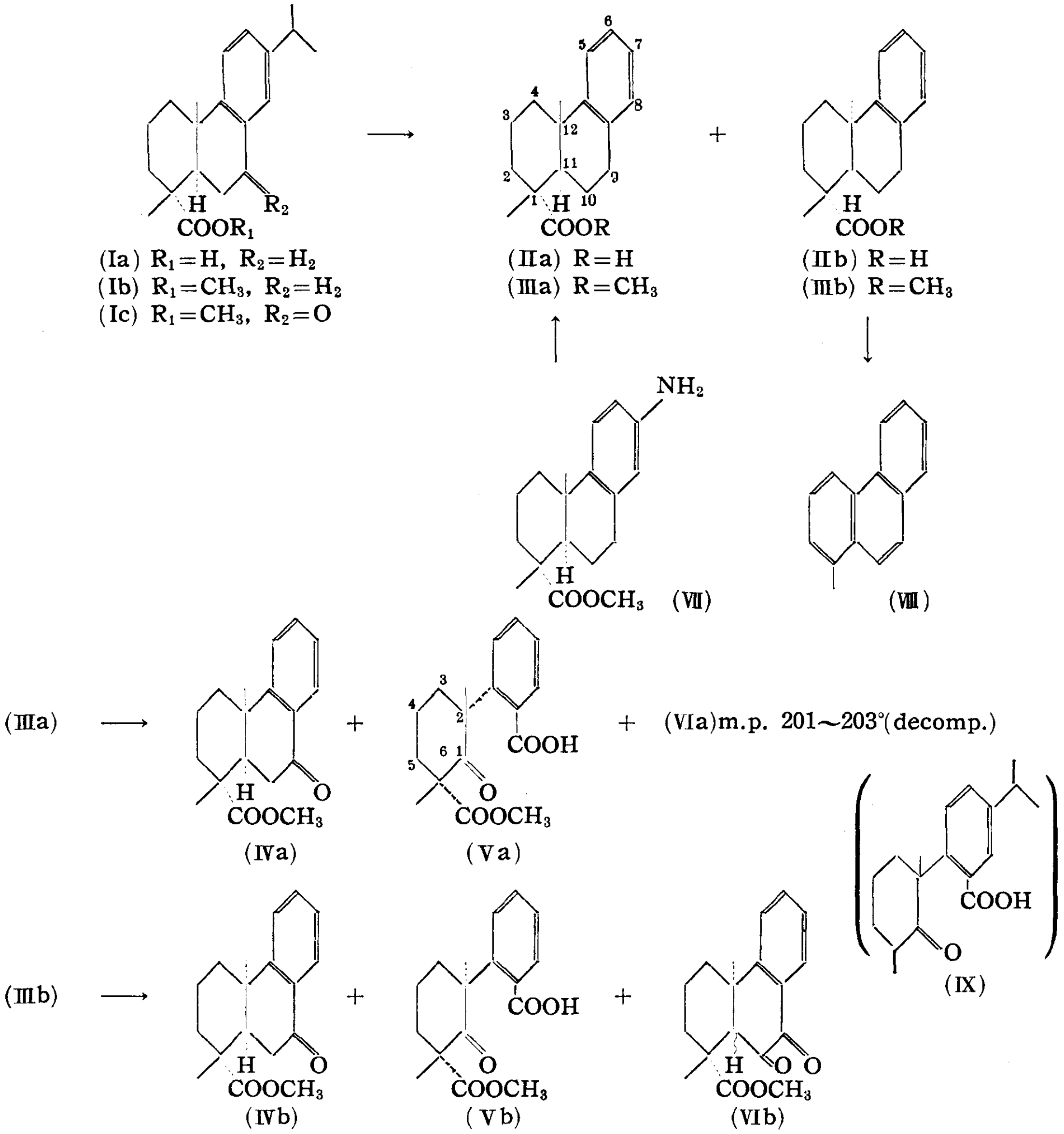
[3] P. F. Ritchie, *et al.* : J. Am. Chem. Soc., **75**, 2610(1953).
[4] H. H. Zeiss, *et al.* : *Ibid.*, **77**, 6707(1955).



(Ia) $R_1=H$, $R_2=H_2$
(Ib) $R_1=CH_3$, $R_2=H_2$
(Ic) $R_1=CH_3$, $R_2=O$

(IIa) R=H
(IIIa) $R=CH_3$

(IIb) R=H
(IIIb) $R=CH_3$

(VII)

(VIII)

(IIIa) ⟶ (IVa) + (Va)

(IX)

(IIIb) ⟶ (IVb) + (Vb) + (VIb)

at 284 mμ as an aromatic carboxylic acid, it is certain that (Vb) is a steric isomer of (Va).

The analytical values of (VIb) agree with $C_{18}H_{20}O_4$, assumed to be methyl 9,10-dioxodeisopropylallodehydroabietate from the similarity of its ultraviolet spectrum (cf. Fig. 2) to that of (VIa) and its yellow coloration. When 5 moles of chromium trioxide is used for (IIIb), the yield of (VIb) reaches 68% but the use of 8.2 moles in this case affords (Vb) in 60% yield.

Decreased amount of chromium trioxide failed to yield almost any 9-oxo compound when acetic acid was used as a solvent, forming (VIb) and recovering the starting material. The use of acetic anhydride,[5] in order to suppress the oxidative power of chromium trioxide, afforded the 9-oxo compound (IVb) in the maximum yield of 54%. (IVb) formed a 2,4-dinitrophenylhydrazone of m.p. 194°, and its structure seems certain from its ultraviolet spectrum (cf. Fig. 1) and molecular rotation (M_D −212).

The fact that (IIIa) normally affords the 9-oxo compound when the amount of chromium trioxide is adjusted, while (IIIb) is easily oxidized to the 9,10-dioxo compound when acetic acid is used as a solvent, is interesting in connection with the configurations of A−B rings.

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[5] T.M. Sanderson, *et al.* : J. Am. Chem. Soc., **78**, 630(1956).

The present series of work was carried out under the kind guidance of Prof. Eiji Ochiai of the University of Tokyo to whom the writers are greatly indebted. Gratitute is expressed to Mr. Yoshiki Matsui of the Shionogi Research Laboratory for infrared spectral measurements and to the members of the Analysis Room of this Laboratory for elemental analyses.

Experimental[6]

Deisopropylation of Dehydroabietic Acid (Ia)—To a solution of 12 g. of (Ia) dissolved in 360 cc. of dehyd. benzene, 12 g. of finely pulverized $AlCl_3$ was added and stirred for 3 hrs., maintaining the temperature of the solution at 30~33°. After decomposition with addition of dil. HCl, benzene layer was separated and extracted with 5% NaOH. The aqueous layer was acidified with HCl, extracted with $CHCl_3$, and after drying over anhyd. Na_2SO_4, $CHCl_3$ was distilled off. The residue was submitted to low-pressure distillation and 7.97 g. of yellowish, vitreous fraction,[7] b.p$_{3\sim4}$ 193~196°, was obtained. This fraction was dissolved in 48 cc. of isopropyl ether with warming, 4.9 g. of diisoamylamine was added, and allowed to stand, from which 8.45 g. of needles, m.p. 149~150°, were obtained. This substance was dissolved in hot MeOH, acidified with 20% AcOH, the liberated acid was collected by filtration, and washed with water. Recrystallization from MeOH afforded 3.5 g. of (IIb), m.p. 157~161°. Concentration of the mother liquor afforded further 1 g. of (IIb), m.p. 157~160°. Total yield, 4.5 g. (44% calcd. from (Ia)). Repeated recrystallization raised the m.p. to 160~162°. *Anal.* Calcd. for $C_{17}H_{22}O_2$: C, 79.0; H, 8.6. Found : C, 78.64; H, 8.68. $[\alpha]_D^{28}$ +1.7°(c=2.956).

The mother liquor left after separation of the salt of (IIb) was evaporated to dryness and the syrupy residue was treated similarly with AcOH. The freed acid was recrystallized from MeOH, affording 0.65 g. of (IIa), m.p. 168~171.5°(yield from (Ia), 6%). Repeated recrystallization raised the m.p. to 171~173°. *Anal.* Calcd. for $C_{17}H_{22}O_2$: C, 79.0; H, 8.6. Found : C, 78.64; H, 8.50. $[\alpha]_D^{28}$ +69.4°(c=2.668).

Methyl Deisopropyldehydroabietate (IIIa)—i) Prepared by the methylation of (IIa) with CH_2N_2 in Et_2O and recrystallized from MeOH to crystals of m.p. 108~109° *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.4; H, 8.9. Found : C, 79.29; H, 8.75. $[\alpha]_D^{25}$ +60.5°(c=2.494). U.V. λ_{max} mμ(log ε) : 265(2.68), 273(2.65).

ii) To a suspension of 0.56 g. of (VII) in 15 cc. of 10% HCl, a solution of 0.2 g. of $NaNO_2$ in small amount of water was added dropwise under stirring and ice chilling, to effect diazotization. This diazotized solution was added dropwise into ice-chilled solution of 18 cc. of 17% NaOH added with 2 cc. of 37% HCHO solution. After 10 mins., the ice bath was taken away and the mixture was stirred for 1 hr. at the room temperature. This was extracted with Et_2O, the extract was washed with dil. HCl and water, dried over anhyd. Na_2SO_4, and the Et_2O evaporated. The residue was distilled under a reduced pressure and 0.24 g. of a fraction of b.p$_2$ 180~190°(bath temp.) was obtained. Several recrystallizations from MeOH afforded crystals of m.p. 107~108°, undepressed on admixture with (IIIa) obtained by the former method. *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.4; H, 8.9. Found : C, 79.28; H, 8.82. $[\alpha]_D^{22}$ +60.2°(c=1.494).

Methyl Deisopropylallodehydroabietate (IIIb)—Prepared by the methylation of (IIb) with CH_2N_2 and recrystallized from MeOH to crystals of m.p. 93~94°. *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.4; H, 8.9. Found : C, 79.17; H, 8.70. $[\alpha]_D^{20}$ −5.1°(c=2.944). U.V. λ_{max} mμ(log ε) : 265(2.65), 273(2.62).

Oxidation of (IIIa) with CrO_3—i) To a solution of 2 g. (7.35 m.moles) of (IIIa) dissolved in 20 cc. of glacial AcOH, a solution of 2 g. (20 m.moles) of CrO_3 dissolved in a mixture of 2 cc. of water and 10 cc. of glacial AcOH was added dropwise under stirring, maintaining the solution at 60~70°, and the mixture was heated for 6 hrs. at 75~80°. After standing over night at room temperature, MeOH was added to the mixture, the solvent was distilled off under a reduced pressure, and the residue was added with water. This was extracted with Et_2O, the Et_2O extract was extracted with 10% Na_2CO_3, and the alkaline solution was acidified with HCl. This was again extracted with Et_2O, the extract was dried over anhyd. Na_2SO_4, and the solvent was evaporated. The residue was recrystallized from MeOH to 0.03 g. (1%) of (Va), m.p. 150~152°.

The Et_2O solution left after extraction with Na_2CO_3 was dried over anhyd. Na_2SO_4, majority of Et_2O was evaporated, and petr. ether added to the residue. The yellow prismatic crystals that precipitated out were collected by filtration and recrystallized from benzene to 0.23 g. (10%) of (VIa), m.p. 201~203°(decomp.). *Anal.* Calcd. for $C_{18}H_{20}O_5$: C, 68.3; H, 6.4. Found : C, 67.87; H, 6.20.

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6) All m.p.s are uncorrected. Optical rotation was measured in EtOH solution with a 1-dm. tube, ultraviolet spectra in EtOH, and infrared spectra in Nujol.

7) By triturating with petr. ether, it undergoes immediate crystallization to m.p. 136~140°, $[\alpha]_D^{14}$ +21.8°(c=1.746).

U.V. λ_{max} mμ(log ε) : 285(3.85), 445(1.68). I.R. λ_{max} : 3.01, 5.76, 5.94 μ.

The mother liquor left after removal of (VIa) was evaporated to dryness, the syrupy residue(1.6 g.) was treated with the Girard-P reagent in a usual manner, and 1.25 g. (60%) of (IVa), b.p$_3$ 198~200°, was obtained. This underwent crystallization on standing to crystals of m.p. 51~53°. *Anal.* Calcd. for $C_{18}H_{22}O_3$: C, 75.5; H, 7.7. Found : C, 75.25; H, 7.85. $[\alpha]^{27}_{D}$ +4.5°(c=5.750). U.V. λ_{max} mμ (log ε) : 253(4.10), 295(3.31).

ii) To a solution of 1 g.(3.68 m.moles) of (IIIa) dissolved in 10 cc. of glacial AcOH, a solution of 2.5 g.(25 m.moles) of CrO_3 dissolved in a mixture of 2.5 cc. of water and 10 cc. of glacial AcOH was added dropwise under stirring at 70°, and the mixture was heated for 7.5 hrs. at 80°. After standing over night, the mixture was treated as in the foregoing section (i) and 0.16 g. (14%) of (VIa), m.p. 200~202°(decomp.), was obtained from the neutral portion. The acid portion was recrystallized from MeOH to 0.72 g. (65%) of (Va), m.p. 151~152°. *Anal.* Calcd. for $C_{17}H_{20}O_5$: C, 67.1; H, 6.6; OCH_3, 10.2; neutr. equiv., 304. Found : C, 66.82; H, 6.80; OCH_3, 10.23; neutr. equiv., 305. $[\alpha]^{25}_{D}$ −8.4° (c=2.378). U.V. λ_{max} mμ(log ε) : 239(3.96), 285(3.20).

Dehydrogenation of (IIb) with Selenium—A mixture of 0.2 g. of (IIb) and 0.25 g. of Se was heated at 300° for 5 hrs. and at 340~350° for 2 hrs. This was treated as usual and recrystallization (with activated C) from MeOH afforded 0.14 g. (94%) of (VIII), m.p. 122°. *Anal.* Calcd. for $C_{15}H_{12}$: C, 93.7; H, 6.3. Found : C, 93.28; H, 6.67.

Picrate : m.p. 137~139°(from EtOH). Both (IIb) and its picrate showed no depression of m.p. on admixture with 1-methylphenanthrene and its picrate prepared by the method of Haworth.[8]

Oxidation of (IIIb) with CrO_3—i) To a solution of 3 g. (11 m.moles) of (IIIb) dissolved in 60 cc. of Ac_2O, 1.5 g.(15 m.moles) of CrO_3 was added in small portions during 3 hrs., while stirring the mixture at room temperature. After stirring the mixture for further 3 hrs., it was allowed to stand for 15 hrs. at room temperature and treated as in the case of (IIIa), from which a small amount of yellow crystals (VIb) and 1.71 g. (54%) of (IVb), b.p$_4$ 192~194°, were obtained. *Anal.* Calcd. for $C_{18}H_{22}O_3$(IVb) : C, 75.5; H, 7.7. Found : C, 74.82; H, 7.94. $[\alpha]^{19}_{D}$ −78.9°(c=2.168). U.V. λ_{max} mμ (log ε) : 254(4.07), 296(3.31).

2,4-Dinitrophenylhydrazone : Orange yellow needles (from AcOEt), m.p. 193~194°. *Anal.* Calcd. for $C_{24}H_{26}O_6N_4$: C, 61.8; H, 5.6. Found : C, 61.61; H, 5.62.

ii) The same oxidation as for (IIIa) was carried out on 2.2 g.(8.08 m.moles) of (IIIb) with 4 g.(40 m.moles) of CrO_3 in AcOH (heated at 60° for 2 hrs. and stood at room temp. over night) and the neutral portion (2.24 g.) was recrystallized from benzene-petr. ether to 1.66 g.(68%) of yellow crystals (VIb), m.p. 135~138°. *Anal.* Calcd. for $C_{18}H_{20}O_4$: C, 72.0; H, 6.7. Found : C, 71.75; H, 6.69. U.V. λ_{max} mμ(log ε) : 290(3.86), 445(1.57). I.R. λ_{max} : 5.80, 5.94 μ.

iii) Oxidation of 1 g. (3.68 m.moles) of (IIIb) with 3 g. (30 m.moles) of CrO_3 in AcOH (heated at 85° for 6.5 hrs., left over night at room temp.) was carried out, MeOH was added to the mixture, the solvent was distilled off, and the residue, added with water, was extracted with Et_2O. The ethereal layer was extracted several times with 10% Na_2CO_3, and the ethereal layer was treated as in the foregoing (ii), from which 0.05 g.(4%) of (VIb), m.p. 133~137°, was obtained.

The aqueous layer was acidified with HCl, extracted with Et_2O, and Et_2O evaporated after drying over anhyd. Na_2SO_4. Recrystallization of the residue from MeOH yielded 0.67 g.(60%) of (Vb), m.p. 128~131.5°. *Anal.* Calcd. for $C_{17}H_{20}O_5$: C, 67.1; H, 6.6; OCH_3, 10.2; neutr. equiv., 304. Found : C, 67.21; H, 6.73; OCH_3, 9.95; neutr. equiv., 289. $[\alpha]^{25}_{D}$ −35.4°(c=2.996). U.V. λ_{max} mμ(log ε) : 238 (3.97), 284(3.19).

Summary

Treatment of dehydroabietic acid (Ia) with aluminum chloride in benzene affords two kinds of deisopropylated compound, (IIa) of m.p. 173° and (IIb) of m.p. 162°. The fact that the former possesses the same steric configuration as that of (Ia) was determined and some examinations were made on the chromium trioxide oxidation products of their methyl esters.

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8) R.D. Haworth : J. Chem. Soc., **1932**, 1125.