with dil. hydrochloric acid and extracted with ether. Evaporation of ether gave an oil which showed the IR-spectrum identical with that of Va.

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Total Synthesis of dl-Deguelin

(Synthesis of Rotenoids V)

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Starting with resorcinol, the total synthesis of dl-deguelin (VI) was accomplished. In the course of this investigation, dihydrodeguelic acid (II), dihydroisodeguelic acid (X), dihydro-dehydrodeguelin (III), dehydrodeguelin (IV), dl-deguelol (V) and dihydro-β-rotenonone (XI) were prepared. But the reduction of dihydrodehydrodeguelin (III) to dihydrodeguelin (XII) resulted in failure. The preparation of dihydrodeguelol (XIIIa), its acetate (XIIIb) and dihydro-desoxy-Δ11-dehydrodeguelin (XIV) was also described.

Deguelin (VI) is a representative one of rotenoids which were defined as such compounds as contain a chromanochromanone structure (a fused four rings system B, C, D, E in VI) in the molecule and have more or less insecticidal activity. It was first isolated by E. P. Clark from the root of derris or cube (3), and proved to have the structure VI (4), but the total synthesis of deguelin has remained unaccomplished. Recently M. Miyano et al. (5) has succeeded in the partial synthesis of dl-deguelin from dehydrodeguelin according to a similar method as undertaken on the reduction of dehydrorotenone to rotenone (6).

This paper is concerned with the synthesis of dehydrodeguelin (IV) and the subsequent reduction to dl-deguelin (VI). Although the most feasible route to dehydrodeguelin (IV) appeared to involve deguelic acid (IX) as a key intermediate, the Houben-Hoesch' condensation of β-tubanol (VII) (2) with methyl 2-cyanomethyl-4,5-dimethoxy-phenoxyacetate (VIII) (7) resulted unfortunately only in the formation of a resinous matter and did

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1) Communicated briefly in this Journal, 24, 327 (1960).
4) E. P. Clark, ibid., 54, 2000 (1932).
not attain the purposes of preparing the acid (IX). Dihydro-β-tubanol (I) was, however, condensed with the nitrile (VIII) to give a crude product\(^8\), which melted within a range between 90–130°C and was separated by fractional recrystallisation into dihydrodehydrodeguelin (III) \(^9\) and dihydroidesdegulic acid (X) \(^11\). From the former acid dihydro-

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\(^8\) On treatment of this crude product, even without further purification, with acetic anhydride and sodium acetate, dihydrodehydrodeguelin (III) was also easily obtained from the resulting mixture because of its insolubility. (cf. Experimental).


\(^10\) E.P. Clark, ibid., 53, 2369 (1931).

dehydrodeguelin (III) was obtained by heating with acetic anhydride and sodium acetate.

The dehydration of dihydrodehydrodeguelin (III) to dehydrodeguelin (IV) was achieved by the bromination followed by the dehydrobromination but in a low yield. A mixture of dihydrodehydrodeguelin and N-bromosuccinimide was refluxed in carbon tetrachloride and the reaction was completed in a short period of time. After washing the resulting solution with sodium bicarbonate solution a soluble substance was obtained along with a large quantity of insoluble yellow crystals. The soluble substance was converted by treatment with alcoholic potassium hydroxide to dehydrodeguelin (IV). On the other hand the insoluble crystals were recrystallized from acetic acid and melted at 295~302°C. The compound was established to be dihydro-β-rotenonone (XI) \(^{12}\) from its analysis as well as IR-spectrum.

Dehydrodeguelin (IV) was reduced with sodium borohydride in dioxane to dl-deguelol (V) \(^5\), m. p. 180~180.5°C, the structural assignment of which was consistent with its IR-spectroscopic and analytical data. dl-Deguelol was oxidized in benzene solution with aluminum isopropanoxide and acetone to dl-deguelin (VI), m. p. 167~168°C, which was identical to the authentic sample isolated from derris roots. Thus the total synthesis of dl-deguelin was first accomplished through twelve steps starting with resorcinol.

A possible approach to dihydrodeguelin (XII) other than the catalytic hydrogenation\(^4,^{13}\) of deguelin (VI) would be achieved from dihydrodehydrodeguelin (III) by a similar procedure as for the reduction of dehydrodeguelin (IV). Unfortunately the reduction of dihydrodehydrodeguelin (III) with sodium borohydride did not proceed, in dioxane, probably owing to its low solubility, while in methylene chloride, in which it was much more soluble, the reduction proceeded but afforded unexpectedly a compound which did not melt even over 300°C and appeared to be an alcohol-boron adduct. When refluxed in alcoholic hydrochloric acid, the adduct was converted not to the expected dihydrodeguelol (XIIIa) but to dihydro-desoxy-Δ"-dehydrodeguelin (XIV), m. p. 167~168°C. In order to gain some informations about the properties of dihydrodeguelol, it was prepared from dihydrodeguelin (XII) by the reduction with lithium aluminum hydride and melted at 153~154°C. It was acetylated to the acetate (XIIIb), m. p. 110~111°C, and dehydrated readily to dihydro-desoxy-Δ"'-dehydrodeguelin (XIV) with either alcoholic hydrochloric acid or acetic anhydride. Consequently for the hydrolysis of the adduct mentioned above to dihydrodeguelol (XIIIa) a mild condition should be required, under that the resulting dihydrodeguelol does not suffer from dehydration to XIV, but it has never been attained.

**EXPERIMENTAL**\(^{14}\)

**Dihydrodeguelic Acid (II) and Dihydroisodeguelic Acid (X)**

A mixture of dihydro-β-tubanol (I) \(^{4,13}\) (800 mg), methyl 4,5-dimethoxy-2-cyanomethylphenoxyacetate (VIII) \(^7\) (1.6 g), zinc chloride (4 g) and anhydrous ether (100 ml) was saturated with hydrogen chloride in two hours (stirring, cooling with ice water). The resulting reddish orange colored solution was allowed to stand at room temperature for three days. After adding ether (100 ml) and standing for additional one hour, the upper ethereal layer was decanted and the reddish viscous oil was washed with ether, heated with water (50 ml) on a water-bath for two hours and extracted with ethyl acetate (3~50 ml). After washing with water and dried over anhydrous sodium sulfate, the extract was evaporated to give a reddish brown viscous oil (1 g), which was added into 1% alcoholic potassium hydroxide (10 ml), refluxed for 40 min, acidified with dil. hydrochloric acid, and extracted with ether. From the ethereal solution the

\(^{13}\) S. Takei, S. Miyajima und M. Ohno, *Ber.*, 66, 1826 (1933).
\(^{14}\) All melting points were uncorrected.
acidic matter was extracted with sodium bicarbonate solution and obtained by acidification followed by extraction with ether as a pale brown solid (600 mg), which was dissolved in 60% aqueous methanol and allowed to stand in a refrigerator overnight. Pale brown needles (350 mg), m.p. 90–130°C, were obtained and recrystallized three times from aqueous methanol to give dihydrodeguelic acid (II) as colorless slender needles (60 mg), m.p. 148–149°C. The mixed melting point showed no depression on admixture with the authentic sample11). Anal. Found: C, 64.11; H, 6.14, Calcd. for C23H26O8: C, 64.17; H, 6.09%.

The evaporation of the combined mother liquors gave brown crystals, which was purified by recrystallization from aqueous methanol to give dihydroiso-deguelic acid (X) (250 mg), m.p. 188°C. The acid was confirmed to be identical to the authentic sample11) by the mixed melting point test and IR-spectra. Anal. Found: C, 64.50; H, 5.85. Calcd. for C23H26O8: C, 64.17; H, 6.09%.

Dihydrodehydrodeguelin (III)

a) A mixture of dihydrodeguelic acid (II) (500 mg), anhydrous sodium acetate (200 mg), acetic anhydride (10 ml) and glacial acetic acid (0.5 ml) was heated for twelve minutes on an oil-bath (150°C). After cooling, water was added and allowed to stand for two hours. The separating crystals (200 mg), m.p. 248–256°C, were collected and recrystallized from ethanol-chloroform (3:2) mixture (80 ml) to give III (180 mg) as faintly yellow plates, m.p. 262–265°C (decomp.), IR-spectrum of which was identical to that of the authentic specimen13). Anal. Found: C, 69.79; H, 5.51. Calcd. for C23H20O7: C, 67.64; H, 4.94%.

b) When a crude mixture of II and X (200 mg), which was obtained above and melted at 90–130°C, was treated according to a similar procedure as in (a), crude III (30 mg), m.p. 230–245°C (decomp.), was obtained. On recrystallization from ethanol-chloroform mixture the melting point was raised to 260–264°C (decomp.).

Dihydro-β-rotenonone (XI) and Dehydrodeguelin (IV)

A mixture of dihydrodehydrodeguelin (III) (500 mg), N-bromosuccinimide (260 mg), benzoyl peroxide (20 mg) and carbon tetrachloride (500 ml) was refluxed for twenty minutes. In ten minutes insoluble crystals were gradually dissolved and finally the color of the solution changed suddenly to fluorescent yellowish green. After cooling, the resulting solution was washed with sodium bicarbonate solution and kept to stand for one hour, bright yellow crystals (280 mg) separated, recrystallized from acetic acid to give dihydro-β-rotenonone (XI), m.p. 295–302°C, (lit., m.p. 310°C10), which showed a IR-spectrum identical to that of the authentic sample prepared from dihydrodeguelin by the oxidation with chromic anhydride. Anal. Found: C, 67.29; H, 5.21. Calcd. for H23H20O7: C, 67.64; H, 4.94%.

Evaporation of the filtrate afforded a brown solid (160 mg), which was extracted with hot ethanol (40 ml) to remain insoluble XI (20 mg). To the extract 5% alcoholic potassium hydroxide was added and allowed to stand overnight. The separating crystals were recrystallized from ethanol to dehydrodeguelin (IV) (28 mg), as pale yellow feather-like crystals, m.p. 225–227°C, IR-spectrum of which was identical to that of the authentic sample13).

dl-Deguelol (V)

Into a mixture of dehydrodeguelin (IV) (2.2 g) and dioxane (80 ml), sodium borohydride (400 mg) in ethanol (20 ml) was added and warmed at 70–75°C for one hour with constant stirring and allowed to stand at room temperature overnight. In order to decompose an excess of sodium borohydride, acetone (30 ml) was added and the solution was kept to stand for four hours. The resulting solution was evaporated in a vacuum to give an oil, which was extracted with chloroform, washed with water, dried over anhydrous potassium carbonate and evaporated. The obtained brown viscous oil was induced to crystallize with a small amount of chloroform-hexane mixture and recrystallized from aqueous acetone to afford V (500 mg) as colorless plates, m.p. 180–180.5°C. Anal. Found: C, 69.59; H, 6.01. Calcd. for C23H24O6: C, 69.69; H, 6.06%.

dl-Deguelin (VI)

A mixture of dl-deguelol (V) (350 mg), benzene (40 ml), acetone (30 ml) and aluminum isopropoxide (3.5 g) was refluxed for ten hours. The resulting yellow mixture was washed with dil. sulfuric acid and with water. Removal of the solvent gave yellow crystals, which was recrystallized from ethanol to afford dl-deguelin (200 mg), as pale yellow prisms, m.p. 167–168°C. Anal. Found: C, 70.05; H, 5.70. Calcd. for C23H22O6: C, 70.05; H, 5.58%.

Dihydrodeguelol (XIIIa)

dl-Dihydrodeguelin (XII) (1 g) in ether (100 ml) was added dropwise into lithium aluminum hydride (600 mg) in ether (100 ml) with stirring and refluxed for one hour. After decomposing an excess of lithium
aluminum hydride with water, dil. hydrochloric acid
was added and dried over anhydrous sodium sulfate.
Removal of ether gave colorless crystals, m.p. 143−
148°C (1 g). The recrystallization from aqueous ace-
tone afforded pure dihydrodeguelol, as colorless prisms,
Calcd. for C_{23}H_{26}O_6: C, 69.35; H, 6.53%.

A mixture of XIIIa (100 mg), acetic anhydride
(5 ml) and pyridine (2 ml) was allowed to stand over-
night at room temperature and poured into water.
On isolation with ether, dihydrodeguelol acetate
(XIIIb) (110 mg) was obtained and recrystallized
from ethanol to give colorless crystals, m.p. 110−111°C.
Anal. Found: C, 67.67; H, 6.38. Calcd. for C_{25}H_{28}O_7:
C, 68.18; H, 6.36%.

Dihydro-desoxy-α¹¹-dehydrodeguelin (XIV)

a) Dihydrodeguelol (XIIIa) (100 mg) was dissolved
in a mixture of conc. hydrochloric acid (0.5 ml) and
ethanol (10 ml) by slightly warming and allowed to
stand overnight. On cooling with ice salt mixture
for five hours, XIV separated and was collected, re-
crystallized from aqueous acetone, colorless crystals
(60 mg), m.p. 167−168°C. Anal. Found: C, 71.57; H,
6.31. Calcd. for C_{23}H_{24}O_5: C, 71.72; H, 6.57%.

b) A mixture of dihydrodeguelol (100 mg) and
acetic anhydride (5 ml) was warmed at 110−115°C
on an oil-bath for four hours and poured into ice
water. The separating oil was extracted with ether,
washed with water, and dried over anhydrous sodium
sulfate. Removal of ether gave brown crystals, which
were recrystallized from aqueous acetone to give XIV
(50 mg).

Reduction of Dihydrodeguelin with Sodium Borohy-
dride

Sodium borohydride (500 mg) in ethanol (30 ml)
was added to dihydrodehydrodeguelin (III) (1.3 g) in
methylene chloride (250 ml) and refluxed for one hour
and allowed to stand overnight at room temperature.
After adding acetone (100 ml) and standing for four
hours, the solvent was removed in a vacuum and the
residue was crystallized from chloroform hexane mix-
ture to give yellow crystals (1.1 g), which did not
melt even over 300°C.

The crystals (800 mg) were heated under reflux in
4% alcoholic hydrochloric acid (30 ml) for three
hours. The resulting solution was evaporated to one
third volume and water was added. The separating
crystals (500 mg), m.p. 133−139°C, were collected,
recrystallized from aqueous acetone to give XIV, m.p.
165−167°C.

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