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# DITERPENOID TOTAL SYNTHESIS—XI*

## (±)-4-EPIDEHYDROABIETIC ACID (CALLITRISIC ACID)

K. Mori and M. Matsui

Department of Agricultural Chemistry, The University of Tokyo,
Bunkyo-ku, Tokyo, Japan

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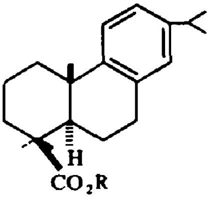
**Abstract**—The synthesis of (±)-4-epidehydroabietic acid is described.

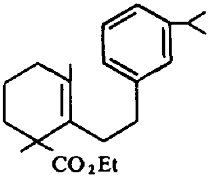
Recently a new resin acid was isolated from *Callitris columellaris* resin by Carman and Deeth.[1] Gough[2] also isolated the acid from *Callitris* resin and named it callitrisic acid. Spectroscopic studies combined with chemical transformations revealed that the new acid is (+)-4-epidehydroabietic acid (Ia).[1,2]

The total synthesis of the racemic acid (Ia) had been achieved by Haworth and Barker[3] in as early as 1939 by the ring-closure of an unsaturated ester (II).† Sharma, *et al.*[4] reported an alternate similar synthesis of the racemate (Ia) in 1963.

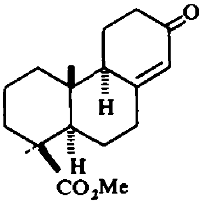
As a part of our efforts to synthesize diterpenes with an axial carboxyl group at C-4, we planned another approach to the racemic acid (Ia) starting from the previously described keto ester (III).[5] Quite independently Carman converted agathic acid (IV) into the (+)-ester (Ib) via the optically active keto ester (III). This note describes the experimental details of our work which has been briefly reported as part of a joint communication from the two laboratories.[6]



Ia: R = H
b: R = Me



II



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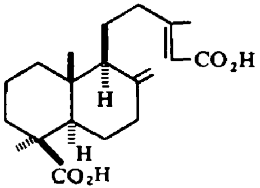

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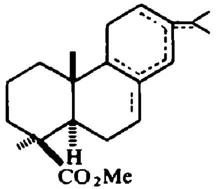
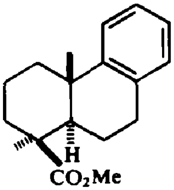


V



VI

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* Part X, R. M. Carman, H. C. Deeth, R. A. Marty, K. Mori and M. Matsui, *Tetrahedron Letters* 3359 (1968).

† Since we have confirmed that the cyclization of this type of compounds by means of sulphuric acid–acetic acid generates acids with *trans* fused A/B rings,[4] it is almost certain that their product possesses the required stereochemistry.

Treatment of the keto ester (III) with isopropyl magnesium bromide afforded a mixture of methyl (±)-4-epiabietate and its isomer (V) after dehydration by acid.[7] The crude product was heated at 230–240° with Pd–C to effect disproportionation.[8] After chromatographic separation methyl (±)-4-epidehydroabietate (Ib) was obtained in 40·5% yield from the keto ester (III). This was identified with the (+)-ester (Ib) by spectral comparisons. Hydrolysis of the racemic ester (Ib) with potassium t-butoxide in DMSO[9] gave the racemic acid (Ia). As a by-product in the course of Pd-catalysed disproportionation, a small amount of methyl (±)-desoxypodocarpate (VI)[5] was obtained.

## EXPERIMENTAL

All m.ps are uncorrected.

*A mixture of methyl (±)-4-epiabietate and its isomer* (V). The ester III (1·45 g) in dry benzene (30 ml) was added to a stirred soln of i-PrMgBr prepared from i-PrBr (2·5 g) and Mg (0·48 g) in dry ether (30 ml). The mixture was stirred for 3 hr at room temp and, after treatment with ice water and sat $NH_4Cl$aq was extracted with ether. The organic layer was concentrated *in vacuo*. Treatment of the crude product with methanolic HCl (6 ml conc HCl + 40 ml MeOH) under reflux for 2 hr gave, after conventional work-up, an oily crude V (1·5 g), $\nu_{max}$ (film 1718 s, 1230 s, 1190 s, 1154 s, 1040 m, 990 m, 890 m $cm^{-1}$. This was employed for the next step without further purification.

*Methyl (±)-4-epidehydroabietate* (Ib). The oily V (1·5 g) was heated at 230–240° with 10% Pd–C (150 mg) for 1·5 hr under $N_2$. After cooling, EtOAc was added and the catalyst was removed by filtration. The oil remaining after concentration of the filtrate was chromatographed over alumina (13·5 × 2·5 cm) in n-hexane. Elution with n-hexane afforded the following fractions (200 ml each). No. 1 and 2: oil (82 mg). No. 3 and 4: the desired crystalline ester Ib (607 mg). No. 5: semi-solid mixture of Ib and VI (154 mg). No. 6–9: the crystalline ester VI (95 mg). Finally elution with ether gave an oily ester (368 mg). The ester Ib, obtained in 40·5% yield from III, was recystallized from MeOH to give elongated prisms, m.p. 92–93° (lit.[3] m.p. 91–92°, lit.[4] m.p. 98–99°). $\nu_{max}$ (Nujol) 1728 s, 1610 w, 1490 m, 1230 m, 1182 m, 1147 m, 1140 m, 1130 m, 892 w, 883 w, 816 s. ($CS_2$) 1734 s, 1610 w, 1230 m, 1184 m, 1146 m, 1130 m, 1028 m, 882 m, 818 s $cm^{-1}$; $\lambda_{max}$ (EtOH) 263 (sh.) (430), 268 (650), 277 (750) mμ (ε); δ (ppm from TMS at 100 MHz, $CCl_4$) 0·98 (3H, s), 1·20 (6H, d, $J$ = 7 Hz), 1·24 (3H, s), 2·75 (3H, m), 3·58 (3H, s), 6·75 (1H, s C-14 H) 6·97 (2H, ABq C-11, 12H). The IR spectrum ($CS_2$) was identical with that of the authentic (+)-ester. (Found: C, 80·37; H, 9·23. Calc. for $C_{21}H_{30}O_2$: C, 80·21; H, 9·62%). The ester VI was identified with an authentic sample by IR.

(±)-*4-Epidehydroabietic acid* (Ia). The ester (Ib, 448 mg) was added to a soln of $KOBu^t$ (from 400 mg of K) in DMSO (30 ml). The mixture was heated at 80° for 1 hr and then left to stand at room temp for 2 days. It was diluted with water and extracted with EtOAc to remove neutral impurities. The aqueous layer was acidified with HCl and extracted with EtOAc. The EtOAc soln was washed with $H_2O$, sat NaCl, dried ($MgSO_4$), and concentrated *in vacuo* to give crystalline acid (412 mg, 96%). This was recrystallized from EtOAc to give prisms, m.p. 198–200° (lit.[3] 202–203°, lit.[4] 202°); $\nu_{max}$ (Nujol) ~2600 m, 1698 s, 1612 w, 1490 m, 1265 m, ~950 w, 885 m, 818 s; ($CHCl_3$) ~3100, ~2600, 1700 s, 1260 m, 820 $cm^{-1}$ $\lambda_{max}$ (EtOH) 262 (sh.) (360), 268 (550), 276 (630) mμ (ε); δ (ppm from TMS at 100 MHz, $CDCl_3$) 1·10 (3H, s) 1·20 (6H, d, $J$ = 7 Hz), 1·30 (3H, s); 2·76 (3H, m), 6·90 (1H, s), 7·08 (2H, ABq). (Found: C, 79·53; H, 9·19. Calc. for $C_{20}H_{28}O_2$: C, 79·95; H, 9·39%).

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## REFERENCES

[1] R. M. Carman and H. C. Deeth, *Austral. J. Chem.* **20**, 2789 (1967).

[2] L. J. Gough, *Tetrahedron Letters* 295 (1968).

[3] R. D. Haworth and R. L. Barker, *J. Chem. Soc.* 1299 (1939).

[4] M. Sharma, U. R. Ghatak and P. C. Dutta, *Tetrahedron* **19**, 985 (1963).

[5] K. Mori and M. Matsui, *Ibid.* **22**, 879 (1966).

[6] R. M. Carman, H. C Deeth, R. A. Marty, K. Mori and M. Matsui, *Tetrahedron Letters* 3359 (1968).

[7] cf. A. W. Burgstahler and L. R. Worden, *J. Am. Chem. Soc.* **86**, 96 (1964).

[8] cf. E. E. Fleck and S. Palkin, *Ibid.* **59**, 1593 (1937).

[9] F. C. Chang and N. F. Wood, *Tetrahedron Letters* 2969 (1964).