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The Chemistry of Fungi. Part LXVIII.[1] Absolute Configuration of 2-Isopropyl-2-methyl-succinic and -glutaric Acids: Some Resultant Stereochemical Corrections

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(+)-2-Isopropyl-2-methylglutaric acid has been prepared from (+)-2-isopropyl-2-methylsuccinic acid. The absolute configuration of these acids has been defined as *S* by an *X*-ray crystallographic examination of (+)-rubidium 1-methyl 2-isopropyl-2-methylsuccinate.

The repercussions of this definition upon the previously accepted absolute stereochemical assignments of numerous substances related to these acids are discussed.

DURING our synthesis[2] of (+)-3-ethyl-3-methyladipic acid, derived from the degradation of the fungal metabolite, rosenonolactone, we became aware of certain important inconsistencies in the published work concern-

[1] Part LXVII, S. A. Ali, J. W. Powell, and W. B. Whalley, preceding paper.

[2] M. R. Cox, G. A. Ellestad, A. J. Hannaford, I. R. Wallwork, W. B. Whalley, and B. Sjöberg, *J. Chem. Soc.*, 1965, 7257.

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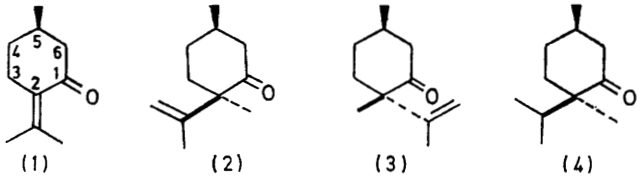
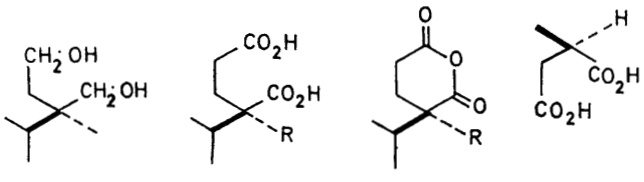
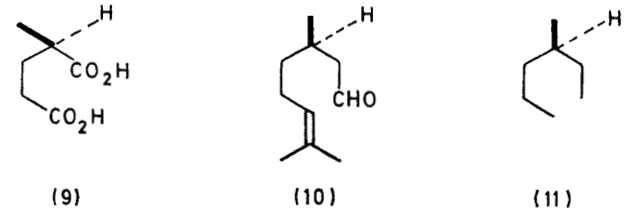
ing the absolute configurations of 2-isopropyl-2-methylsuccinic and 2-isopropyl-2-methylglutaric acids.

Thus, methylation of (+)-pulegone (1) gives, as the major product, (−)-methylisopulegone, which was assigned the absolute configuration (2) by Djerassi *et al.*[3] (−)-Methylpulegone has also been prepared by Kon and Nutland,[4] Conia,[5] and Melera *et al.*,[6] and the Swiss group [6] expressed a preference (without experimental support) for the alternative absolute configuration (3). The absolute configuration (2) was supported [3] by



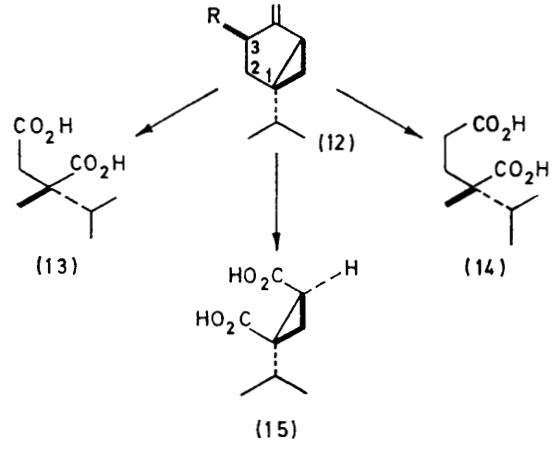




evidence in two parts. In the first, (−)-methylisopulegone was hydrogenated to (+)-dihydromethylisopulegone, formulated as (4), which was degraded to (−)-2-isopropyl-2-methylbutane-1,4-diol. This diol was assigned the *R*-configuration (5) since the antipodal (+)-diol was obtained by reduction of (+)-2-isopropyl-2-methylsuccinic acid.

In the second piece of evidence,[3] (+)-dihydromethylisopulegone was converted into (+)-2-isopropyl-2-methylglutaric acid, which furnished (−)-2-isopropyl-2-methylglutaric anhydride. This acid and anhydride were assigned the *R*-configuration [(6; R = Me) and (7; R = Me), respectively] because they were related to (+)-(*R*)-2-isopropylglutaric acid (6; R = H) and its anhydride (6; R = H), by use of the quasi-racemate technique. The absolute configuration at C-5 in the various derivatives of (+)-pulegone has been established [7] by degradation to (+)-methylsuccinic acid (8) and receives collateral support from (*a*) the correlation [8] of (+)-pulegone with (+)-3-methyladipic acid (9), and (*b*) the correlation [9] of (+)-pulegone with (+)-citronellal (10) and (+)-3-methylhexane (11).

However, this apparent definition of (+)-2-isopropyl-2-methylsuccinic acid as *R* is at variance with the work of Norin,[10] whose investigations produced the opposite conclusion. Thus, in the establishment of the absolute configuration at C-1 in the thujane group of terpenes, Norin [10] degraded (+)-sabinol (12; R = OH) to (+)-2-isopropyl-2-methylsuccinic acid (13); (+)-sabinene (12; R = H) gave (+)-2-isopropyl-2-methylglutaric acid (14). Since (+)-sabinol and (+)-sabinene give the same (+)-α-thujadicarboxylic acid (15) on oxidation,[11] they differ only at C-3; hence Norin concluded [10] that (+)-2-isopropyl-2-methylsuccinic acid (13) and (+)-2-isopropyl-2-methylglutaric acid (14) have the same (*S*) configuration. Collateral support for this conclusion was provided by other interconversions [12,13] of (−)-umbellulone (16), another terpene of the thujane group, and by the correlation of (+)-pulegone with (+)-*cis*- (17) and (+)-*trans*-thujane (18), and with (+)-isothujyl alcohol and (+)-isothujone, and with the sabinenes.[14]



In view of the ramifications of this important discrepancy it was clearly necessary to define, unequivocally, the absolute configurations of (+)-2-isopropyl-2-methylsuccinic acid, (+)-2-isopropyl-2-methylglutaric acid, and their derivatives. A review [15] indicates that these two acids have been correlated chemically, but no details are given.

By partial hydrolysis, (±)-dimethyl 2-isopropyl-2-methylsuccinate [16] was converted into (±)-1-methyl hydrogen 2-isopropyl-2-methylsuccinate (19) which we

[3] C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *J. Amer. Chem. Soc.*, 1961, **83**, 4433; C. Djerassi, F. Burian, E. J. Eisenbraun, and J. Osiecki, *ibid.*, 1960, **82**, 3476.
[4] G. A. R. Kon and J. H. Nutland, *J. Chem. Soc.*, 1926, 3101.
[5] J. M. Conia, *Bull. Soc. chim. France*, 1954, 943.
[6] A. Melera, D. Arigoni, A. Eschenmoser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1956, **39**, 441.
[7] J. von Braun, and F. Jostes, *Ber.*, 1926, **59**, 1444.
[8] E. J. Eisenbraun and S. M. McElvain, *J. Amer. Chem. Soc.*, 1955, **77**, 3383.
[9] See K. Freudenberg and W. Lwowski, *Annalen*, 1954, **587**, 213.
[10] T. Norin, *Acta Chem. Scand.*, 1962, **16**, 640.
[11] F. W. Semmler, *Ber.*, 1900, **33**, 1460; 1902, **35**, 2047.
[12] H. M. Walborsky, T. Sugita, M. Ohno, and Y. Inouye, *J. Amer. Chem. Soc.*, 1960, **82**, 5255.
[13] H. E. Smith and A. W. Gordon, *J. Amer. Chem. Soc.*, 1962, **84**, 2840; E. H. Massey, H. E. Smith, and A. W. Gordon, *J. Org. Chem.*, 1966, **31**, 684; H. E. Smith, J. C. D. Brand, E. H. Massey, and L. J. Durham, *ibid.*, p. 690.
[14] G. Ohloff, G. Uhde, A. F. Thomas, and E. sz. Kovats, *Tetrahedron*, 1966, **22**, 309.
[15] T. Norin, *Svensk kem. Tidskr.* 1964, **76**, 97.
[16] J. Porath, *Arkiv Kemi*, 1949, **1**, 385.

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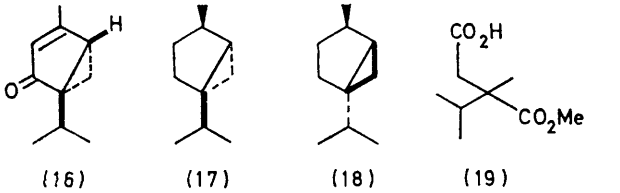
resolved, using dehydroabietylamine,[17] into the (+)- and (−)-half-esters. The rubidium salt of the (+)-half-ester formed a hydrate having two molecules of salt and five



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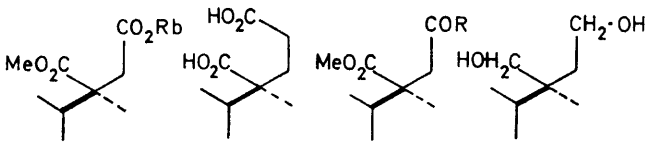


(20) (21) (22) (23)

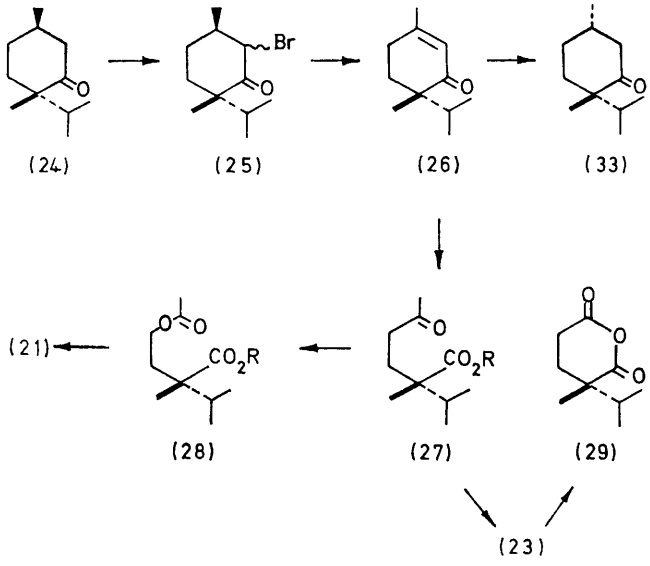
molecules of water per unit cell.[18] An *X*-ray crystallographic examination of this salt,[18] by Professor D. Rodgers and Dr. M. B. Hursthouse (who will publish the details separately) defined the absolute configuration as *S* [as in (20)]. (+)-1-Methyl hydrogen 2-isopropyl-2-methylsuccinate (22; R = OH) was then converted into (+)-2-isopropyl-2-methylglutaric acid (21), by way of the acid chloride (22; R = Cl) and the diazo-ketone (22; R = CHN_2) by use of the Arndt–Eistert procedure, the method having been initially established with the (±)-derivatives (see Experimental section). In agreement with these absolute stereochemical assignments (+)-(*S*)-2-isopropyl-2-methylsuccinic acid and (+)-(*S*)-2-isopropyl-2-methylglutaric acid show positive Cotton effects. This is in agreement with the similar curves obtained [19] with (+)-(*S*)-monoalkylsuccinic and glutaric acids which belong to the same stereochemical series.

To complete these correlations (+)-(*S*)-2-isopropyl-2-methylsuccinic acid (13) was reduced with lithium aluminium hydride, to give (−)-2-isopropyl-2-methylbutane-1,4-diol (23); similarly (−)-(*R*)-2-isopropyl-2-methylsuccinic acid formed (+)-(*R*)-2-isopropyl-2-methylbutane-1,4-diol. The diols were characterised as their bis-4-phenylazobenzoates. Finally (+)-2-isopropyl-2-methylglutaric acid was converted into (−)-2-isopropyl-2-methylglutaric anhydride. These results are in agreement with those of Norin,[10] but completely at variance with those reported by Djerassi and his co-workers.[3] The establishment of (+)-2-isopropyl-2-methylsuccinic acid as an absolute standard provides confirmation for the configurations of (+)-isopropylsuccinic acid and hence for (+)-2-isopropylglutaric acid which was used by Djerassi *et al.*[3] in their determination of the configuration of (+)-2-isopropyl-2-methylglutaric acid by the quasi-racemate method. However, no obvious reasons for the errors in Djerassi's work emerge from our investigations.

Our results are in agreement with the production of (−)-2-isopropyl-2-methylsuccinic acid from (−)-camphoronic acid,[20] and the unequivocal definition of the absolute configuration of (+)-3-bromocamphor.[21]

Since (+)-2-ethyl-2-methylsuccinic acid has been related [22] to (+)-2-isopropyl-2-methylsuccinic acid by the quasi-racemate process, satisfactory collateral evidence is provided for the absolute configuration at C-13 in the rosenonolactone group of diterpenes.[23] Additionally, (+)-2-ethyl-2-methylsuccinic acid has been related [22] to (+)-ethylsuccinic acid, which in turn has been related [24] to (+)-propylsuccinic acid. Thus, the absolute stereochemical relationship between numerous lower aliphatic acids and (+)-pulegone has been established by two independent and mutually confirmatory routes. An additional key absolute standard is provided by (+)-methylsuccinic acid, the absolute configuration of which follows from the *X*-ray crystallographic examination of the fungal metabolite, ergoflavin.[25]

The additional consequences of our results may now be examined. Thus the correct configurations of the substances involved in the degradative sequence performed on (−)-methylisopulegone (3) by Djerassi's group [3] are to be written as in (24)—(29). (−)-Methylisopulegone thus has the (2*S*,5*R*)-configuration (3),



(24) (25) (26) (33)

(21) (28) (27) (29)

(23)

whilst (+)-dihydromethylisopulegone [(+)-2-methylmenthone] is (+)-(2*S*,5*R*)-2-isopropyl-2,5-dimethylcyclohexanone (24). The dehydrobromination product from the bromo-ketone (25) (presumably a mixture of epimers) is therefore (−)-(6*S*)-6-isopropyl-2,6-dimethylcyclohex-2-enone (26). The minor product, (+)-methylisopulegone, from the methylation of (+)-pulegone is

[17] *Cf.* ref. 2, and other references cited therein.
[18] M. R. Cox, H. P. Koch, and W. B. Whalley, and M. B. Hursthouse and D. Rogers, *Chem. Comm.*, 1967, 212.
[19] A. Fredga, J. P. Jennings, W. Klyne, P. M. Scopes, B. Sjöberg, and S. Sjöberg, *J. Chem. Soc.*, 1965, 3928.
[20] J. Porath, *Arkiv Kemi*, 1950, **1**, 525.
[21] F. H. Allen and D. Rogers, *Chem. Comm.*, 1966, 838.
[22] J. Porath, *Arkiv Kemi*, 1951, **3**, 163.
[23] A. I. Scott, S. A. Sutherland, D. W. Young, I. Guglielmetti, D. Arigoni, and G. A. Sim, *Proc. Chem. Soc.*, 1964, 19.
[24] M. Matell, *Arkiv Kemi*, 1953, **5**, 17.
[25] A. T. McPhail, G. A. Sim, J. D. M. Asher, J. M. Robertson, and J. V. Silverton, *J. Chem. Soc.* (*B*), 1966, 18; J. W. ApSimon, J. A. Corran, N. G. Creasey, K. Y. Sim, and W. B. Whalley, *Proc. Chem. Soc.*, 1963, 209.

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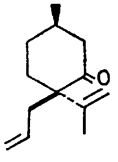
therefore (2) with the (2*R*,5*R*)-configuration, and the hydrogenation product of this is (+)-(2*R*,5*R*)-2-isopropyl-2,5-dimethylcyclohexanone (4).

Because the major product (83%) from the methylation of (+)-pulegone is now defined as (3), the alkylation does not involve any mechanistic problems (contrast Djerassi *et al.*[3]), since alkylation to yield (3) must proceed predominantly by axial approach of the alkylating species, in accord with accepted concepts. Similarly, the major and minor products from the allylation [26] of (+)-pulegone may be formulated as (30) and (31), respectively, and not the reverse as previously.[26]

During additional investigations in the (+)-pulegone series Djerassi *et al.*[3] monomethylated the spirodithian derivative (32); removal of the sulphur ring furnished a ketone now known to be (4). Thus methylation



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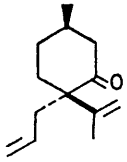

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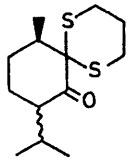

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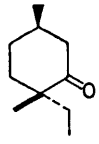

(34)

occurs *trans* to the C-5 methyl substituent, in contrast to the methylation of (+)-pulegone, where methylation occurs predominantly *cis* to the C-5 methyl substituent. Djerassi's group [3] prepared (33) the mirror image of (4), by catalytic reduction of the αβ-unsaturated ketone (26): in contrast to this result reduction of (26) with lithium and liquid ammonia formed (24) as the principal product.

After reduction of the carbonyl group in (−)-methylisopulegone the isopropenyl group was modified [3] to yield (+)-2-ethyl-2,5-dimethylcyclohexanone, which is now to be formulated as (34), with the methyl groups *cis* and having the (2*R*,5*R*)-configuration.

Independent verification of our definition of the absolute configuration of (−)-methylpulegone as (3) is provided by the work of Cookson *et al.*,[27] from c.d. studies.

EXPERIMENTAL

Unless stated otherwise light petroleum refers to the fraction of b.p. 40—60°.

(±)-1-*Methyl Hydrogen* 2-*Isopropyl*-2-*methylsuccinate*.—A solution of dimethyl 2-isopropyl-2-methylsuccinate (36 g) (prepared quantitatively by the action of diazomethane upon 2-isopropyl-2-methylsuccinic acid) in methanol (200 ml) containing potassium hydroxide (10·8 g) was refluxed for 3·5 h. The solvent was evaporated off *in vacuo* and the residue extracted with ether. The residue was then dissolved in the minimum of water and acidified with concentrated hydrochloric acid, and the product was isolated with ether to yield the (±)-half-ester (32 g) as an oil, b.p. 118—120° at 1 mmHg, which was characterised as the anilide.

Thus a solution of the half ester (5·5 g) in benzene (30 ml) containing oxalyl chloride (7 ml) was kept for 2 h, and then refluxed for 0·5 h. Purified by distillation, *methyl* 2-(*chlorocarbonylmethyl*)-2,3-*dimethylbutyrate* formed an oil (3·5 g), b.p. 103—108° at 10 mmHg [Found: C, 53·3; H, 7·5; Cl, 17·0; OMe, 14·25. $C_8H_{12}ClO_2$(OMe) requires C, 52·3; H, 7·3; Cl, 17·2; OMe, 15·0%]. Prepared from this acid chloride the *anilide* separated from ether–light petroleum in needles, m.p. 90° [Found: C, 68·9; H, 8·0; N, 5·4; OMe, 11·6. $C_{14}H_{18}NO_2$(OMe) requires C, 68·4; H, 8·0; N, 5·3; OMe, 11·8%].

(±)-2-*Isopropyl*-2-*methylglutaric Acid*.—A solution of the foregoing acid chloride (6·5 g) in ether (50 ml) was added slowly to an ethereal solution of diazomethane (4·2 g). Four hours later the diazo-ketone (3·6 g) was isolated as a yellow oil and dissolved in dioxan (100 ml). This solution was treated, with stirring, with silver nitrate (0·75 g) in water (15 ml) and ammonia (*d* 0·88; 20 ml), added in small portions. Forty-five minutes later more ammonia (*d* 0·88; 10 ml) was added. After isolation in the normal manner the product was purified by chromatography from benzene–ether (1 : 1) on alumina to yield *methyl* 4-*carbamoyl*-2-*isopropyl*-2-*methylbutyrate* (2 g), which formed pale yellow needles, m.p. 67° (from light petroleum) [Found: C, 59·8; H, 9·6; N, 7·0; OMe, 15·0. $C_9H_{16}NO_2$(OMe) requires C, 59·7; H, 9·5; N, 7·0; OMe, 15·4%].

Hydrolysis of this amide (1·8 g) with boiling 5N-hydrochloric acid during 24 h gave (±)-2-*isopropyl*-2-*methylglutaric acid* (1·1 g), which was initially purified by chromatography from benzene–light petroleum (9 : 1) on silica, and then by crystallisation from ether to yield needles, m.p. 80° (Found: C, 57·3; H, 8·6. $C_9H_{16}O_4$ requires C, 57·4; H, 8·6%). Treatment of this acid (0·1 g) with boiling acetic anhydride (15 ml) during 1 h, followed by removal of the solvent *in vacuo* gave (±)-2-*isopropyl*-2-*methylglutaric anhydride* which separated from chloroform or light petroleum in needles, m.p. 36° (Found: C, 63·3; H, 8·3. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%).

(±)-2-*Isopropyl*-2-*methylbutane*-1,4-*diol*.—A solution of (±)-2-isopropyl-2-methylsuccinic acid (3·76 g) in boiling ether (250 ml) was reduced with lithium aluminium hydride (3·1 g) during 4 h, to yield (±)-2-*isopropyl*-2-*methylbutane*-1,4-*diol* (3·5 g), b.p. 130—134° at 20 mmHg (Found: C, 65·0; H, 12·1. $C_8H_{18}O_2$ requires C, 65·7; H, 12·4%). The *bis*-(4-*phenylazobenzoate*) formed orange plates, m.p. 119° [from light petroleum (b.p. 60—80°)] (Found: C, 72·6; H, 6·1; N, 10·0. $C_{34}H_{34}N_4O_4$ requires C, 72·6; H, 6·1; N, 10·0%). Isolated from the mother liquors remaining after the separation of this bis-(4-phenylazobenzoate), 3-*hydroxymethyl*-3,4-*dimethylpentyl* 4-*phenylazobenzoate* formed orange plates, m.p. 85° [from light petroleum (b.p. 60—80°)] (Found: C, 70·6; H, 7·4; N, 8·1. $C_{21}H_{26}N_2O_3$ requires C, 71·2; H, 7·4; N, 7·9%).

(±)-4-*Methyl Hydrogen* 2-*Isopropyl*-2-*methylsuccinate*.—A solution of (±)-2-isopropyl-2-methylsuccinic acid (5 g) in methanol (25 ml) containing concentrated sulphuric acid (0·5 ml) was refluxed for 2 h. The product was isolated in the normal manner to yield the *half-ester* (3·2 g) in large rhombohedra, m.p. 52° (from light petroleum) [Found: C, 57·3; H, 8·5; OMe, 16·3. $C_8H_{13}O_3$(OMe) requires C, 57·4; H, 8·6; OMe, 16·4%].

[26] J. M. Conia and P. Le Perchec, *Bull Soc. chim. France*, 1966, 273.

[27] R. C. Cookson, J. Hudec, A. Szabo, and G. E. Usher, *Tetrahedron*, 1968, **24**, 4353.

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(+) *and* (−)-1-*Methyl Hydrogen* 2-*Isopropyl*-2-*methylsuccinate*.—A solution of the (±)-half-ester (30·7 g) in ether (100 ml) was added to an ethereal solution (30 ml) of dehydroabietylamine (50 g). The crystalline salt (44 g) which separated during 24 h was collected and repeatedly recrystallised from light petroleum–methanol and light petroleum–chloroform to give the dehydroabietylamine *salt*, m.p. 154° of the (+)-half-ester in needles (26 g), $[\alpha]_D^{25}$ +26·1° (*c* 4·98 in MeOH) (Found: C, 72·8; H, 9·3; N, 3·1. $C_{29}H_{47}NO_4$ requires C, 73·5; H, 10·0; N, 3·0%). This salt (26 g) was shaken with an excess of ice-cold 2N-sodium hydroxide until dissolution was complete; liberated amine was removed by extraction with light petroleum and the residual aqueous solution after evaporation to small volume *in vacuo* was acidified (at 0°) with 10N-hydrochloric acid. After isolation with ether, the (+)-*half-ester* (8·9 g) separated from light petroleum in prisms, m.p. 45°, $[\alpha]_D^{24}$ +11·6° (*c* 5·88 in MeOH), $[\alpha]_D^{24}$ +9·4° (*c* 9·04 in $CHCl_3$) [Found: C, 57·2; H, 8·6; OMe, 16·4. $C_8H_{13}O_3$(OMe) requires C, 57·4; H, 8·6; OMe, 16·4%].

The mother liquors remaining from the purification of the salt of m.p. 154° were evaporated to dryness *in vacuo* and the residue was repeatedly crystallised from light petroleum–methanol and light petroleum–chloroform to yield the dehydroabietylamine *salt* (11 g) in silky needles, m.p. 136° of the (−)-acid, $[\alpha]_D^{25}$ +19·0° (*c* 5·23 in $CHCl_3$) (Found: C, 73·1; H, 10·2; N, 3·0. $C_{29}H_{47}NO_4$ requires C, 73·5; H, 10·0; N, 3·0%). Decomposition of this derivative as for the diastereoisomer gave the (−)-*half-ester* in prisms (from light petroleum), m.p. 47°, $[\alpha]_D^{24}$ −10·0° (*c* 12·2 in $CHCl_3$) [Found: C, 57·5; H, 8·6; OMe, 15·8. $C_8H_{13}O_3$(OMe) requires C, 57·4; H, 8·6; OMe, 16·4%].

Derivatives of (+)-1-*Methyl Hydrogen* 2-*Isopropyl*-2-*methylsuccinate*.—Prepared by the hydrolysis of this ester (1·1 g) with boiling 5N-hydrochloric acid (10 ml) during 10 h, (+)-(*S*)-2-isopropyl-2-methylsuccinic acid formed plates (0·8 g), m.p. 132°, identical with an authentic sample, $[\alpha]_D^{19}$ −0·94° (*c* 10·6 in $CHCl_3$), $[\alpha]_D^{17}$ +16·1° (*c* 8·98 in MeOH).

Obtained by the neutralisation of the corresponding acid with rubidium hydroxide solution (+)-*rubidium* 1-*methyl* 2-*isopropyl*-2-*methylsuccinate* separated from ether–methanol (20 : 1) containing 1% of water, as a hydrate (needles) which showed a phase change at 75—80° and had m.p. 210—220°, $[\alpha]_D^{24}$ +6·7° (*c* 6·34 in MeOH) (Found: C, 33·8; H, 6·2. $C_9H_{15}O_4Rb$,2·5H_2O requires C, 34·1; H, 6·3%).

(+)-2-*Isopropyl*-2-*methylglutaric Acid*.—Prepared by the application of the Arndt–Eistert process to (+)-1-methyl hydrogen 2-isopropyl-2-methylsuccinate as for the (±)-isomer, (+)-2-*isopropyl*-2-*methylglutaric acid* formed prisms, m.p. 70° [from benzene–ether (1 : 1)], $[\alpha]_D^{18}$ +12·0° (*c* 3·27 in $CHCl_3$), $[\alpha]_D^{22}$ +10·5° (*c* 5·0 in MeOH) (Found: C, 57·5; H, 8·8. $C_9H_{16}O_4$ requires C, 57·4; H, 8·6%). This acid furnished (−)-2-*isopropyl*-2-*methylglutaric anhydride*, in flat needles, m.p. 58° (from light petroleum), $[\alpha]_D^{22}$ −57·8 (*c* 4·85 in $CHCl_3$) (Found: C, 63·5; H, 8·5. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%).

(−)-2-*Isopropyl*-2-*methylbutane*-1,4-*diol*.—Reduction of (+)-2-isopropyl-2-methylsuccinic acid with lithium aluminium hydride as for the (±)-isomer, gave (−)-2-isopropyl-2-methylbutane-1,4-diol, $[\alpha]_D^{20}$ −2·01° (*c* 8·90 in $CHCl_3$) (Found: C, 65·4; H, 12·5. $C_8H_{18}O_2$ requires C, 65·7; H, 12·4%). This (−)-diol gave a *bis*-(4-*phenylazobenzoate*) in orange red plates, m.p. 128° (from light petroleum), $[\alpha]_D^{20}$ −11·1° (*c* 2·11 in $CHCl_3$) (Found: C, 71·9; H, 6·0; N, 9·9. $C_{34}H_{34}N_4O_4$ requires C, 72·6; H, 6·1; N, 10·0%).

(+)-2-*Isopropyl*-2-*methylbutane*-1,4-*diol*.—Prepared from (−)-1-methyl hydrogen 2-isopropyl-2-methylsuccinate acid (3·46 g), the (+)-*diol* formed an oil (2·6 g), b.p. 98—105° at 2 mmHg, $[\alpha]_D^{26}$ +2·04° (*c* 12·54 in $CHCl_3$) (Found: C, 65·3; H, 12·5. $C_8H_{18}O_2$ requires C, 65·7; H, 12·4%). The *bis*-(4-*phenylazobenzoate*) formed orange plates, m.p. 128° (from light petroleum), $[\alpha]_D$ +13·9° (*c* 2·26 in $CHCl_3$) (Found: C, 72·6; H, 6·1; N, 9·9. $C_{34}H_{34}N_4O_4$ requires C, 72·6; H, 6·1; N, 10·0%). The *bis*-(4-*iodobenzoate*) formed rosettes of needles, m.p. 82° (from light petroleum or methanol), $[\alpha]_D^{24}$ +5·0° (*c* 8·815 in $CHCl_3$) (Found: C, 43·8; H, 4·0; I, 43·5. $C_{22}H_{24}I_2O_4$ requires C, 43·6; H, 4·0; I, 41·9%).

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