Absolute Configuration of Atrovenetin and Related Compounds

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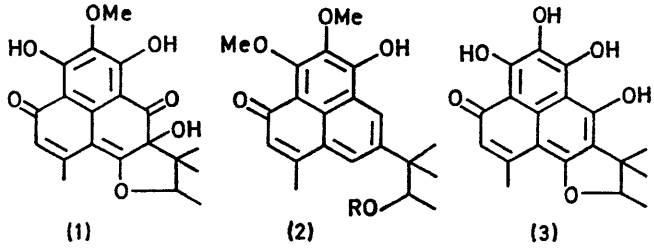
Summary Chemical correlation of a degradation product of isoherqueinone with *S*-(−)-ethyl lactate has established that herqueinone and isoherqueinone have the *R*- and *S*-configuration respectively at the asymmetric centre in the side-chain; it follows that atrovenetin possesses the *R*-configuration.

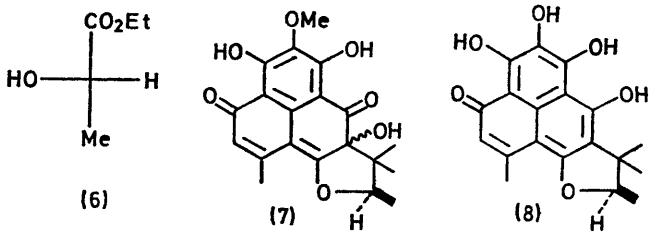
HERQUEINONE (**1**) and atrovenetin (**3**) have the same absolute configuration at the asymmetric centre in the side-chain, while isoherqueinone (which is co-extracted with herqueinone from the mycelium of *P. Herquei*) has the opposite configuration at that centre.[1] This communication describes the determination of the absolute configuration of the asymmetric centre in the side-chain of all three compounds.

Herqueinone and isoherqueinone may be degraded into the (−)- and (+)-enantiomers respectively of the phenalenone (**2**; R = H).[1] We have now oxidised the mono-3,5-dinitrobenzoate [**2**; R = $C_6H_3(NO_2)_2$·CO] of the (+)-enantiomer (**2**; R = H) with ruthenium tetroxide and sodium periodate[2] to (+)-αα-dimethyl-β-(3,5-dinitrobenzoyl)oxybutyric acid [**4**; R = $C_6H_3(NO_2)_2$·CO], $[\alpha]_D$ + 34°.† The same material was also obtained from racemic αα-dimethyl-β-hydroxybutyric acid (**4**; R = H)[3] by resolution of its 3,5-dinitro-



RO·CHMe·CMe_2·CO_2H
(4)

RO·CHMe·CMe_2OH
(5)



benzoate by fractional crystallisation of the diastereoisomeric brucine salts; by this means, the (−)-3,5-dinitrobenzoate [**4**; R = $C_6H_3(NO_2)_2$·CO] was obtained optically pure ([α]$_D$ − 35°†) while the (+)-enantiomer was obtained with a specific rotation of +28°.†

Both enantiomers of αα-dimethyl-β-(3,5-dinitrobenzoyl)-oxybutyric acid were correlated with ethyl lactate as follows. Saponification of the (+)- and (−)-3,5-dinitrobenzoates [**4**; R = $C_6H_3(NO_2)_2$·CO] gave respectively (+)-αα-dimethyl-β-hydroxybutyric acid (**4**; R = H), [α]$_D$ + 7·9°, and its (−)-enantiomer ([α]$_D$ − 9·1°), which were subsequently converted into the (+)- and (−)-acetoxy-acids (**4**; R = Ac) respectively by treatment with pyridine and acetic anhydride at room temperature. The carboxy-group in each of these enantioners was replaced with a hydroxy-group by heating the derived peroxy-acid (obtained by perhydrolysis of the corresponding acid chloride with alkaline hydrogen peroxide[4]) in olefin-free light petroleum.[5] In this way, the (+)-acetoxy-acid (**4**; R = Ac) gave (+)-3-acetoxy-2-methylbutan-2-ol (**5**; R = Ac), [α]$_D$ + 12·2°, while the (−)-acetoxy-acid gave the (−)-diol acetate (**5**; R = Ac), [α]$_D$ − 13·5°. The correlation was completed by treating *S*-(−)-ethyl lactate (**6**), [α]$_D$ − 11·4° (neat) with MeMgI to give (+)-2-methylbutane-2,3-diol (**5**; R = H), [α]$_D$ + 4·0° (neat), b.p. 85° at 19 mmHg (84% yield),‡ acetylation of which gave (+)-3-acetoxy-2-methylbutan-2-ol (**5**; R = Ac), [α]$_D$ + 12·3°.

The above results establish that the laevorotatory enantiomers of compounds (**2**; R = H), [**4**; R = H, Ac, or $C_6H_3(NO_2)_2$·CO], and (**5**; R = H or Ac) all possess the *R*-configuration, while the dextrorotatory enantiomers belong to the *S*-configurational series. The formula of herqueinone may now be expressed as (**7**); isoherqueinone differs from it only in the configuration of the asymmetric centre in the side-chain. Similarly, the complete stereoformula of atrovenetin (extracted from the mycelium of *P. Atrovenetum*) may be written as (**8**) with the asymmetric centre in the *R*-configuration.

Satisfactory analyses and spectra were obtained for all the new compounds described.

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† Acetone solution; unless indicated otherwise all other specific rotations refer to chloroform solutions.

‡ Our present results are at variance with an earlier report[6] that reaction between (−)-ethyl lactate, [α]$_D$ − 9·473° (neat) and 2 mol. equiv. of MeMgI gives (−)-2-methylbutane-2,3-diol (**5**; R = H), [α]$_D$ − 6·965° (neat), b.p. 176—178° at 20 mmHg. These earlier workers quoted no analytical or spectroscopic data to support their assigned structure. Our own observations accord well with a report that treatment of *R*-(+)-methyl lactate with methylmagnesium iodide affords (−)-2-methylbutane-2,3-diol (**5**; R = H).[7]

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