

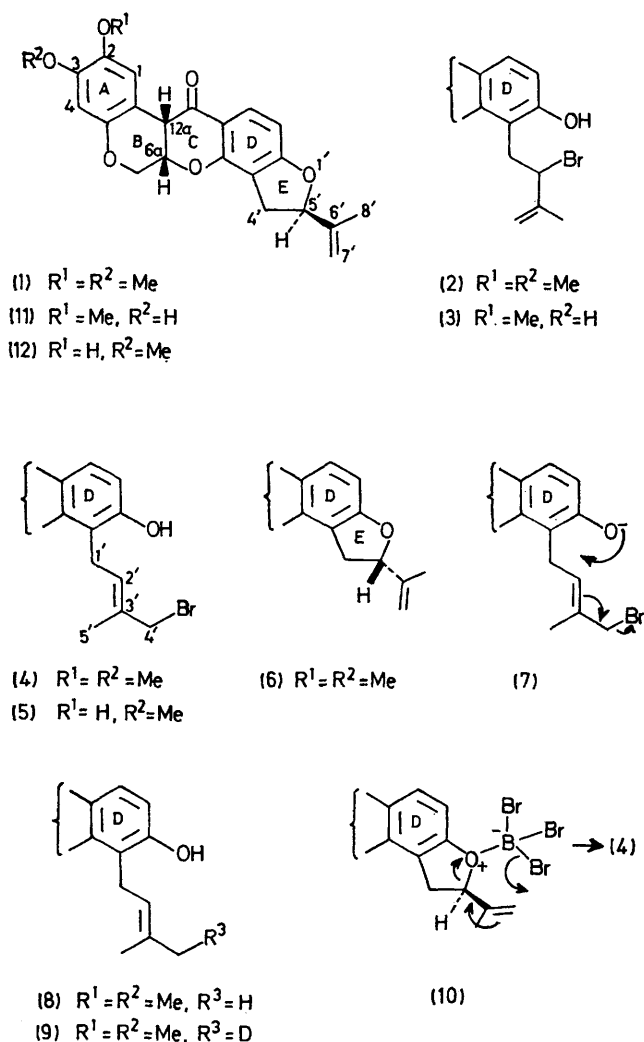
Reaction of Rotenone with Boron Tribromide. Stereospecific ^2H -Labelling of (—)-Rotenonic Acid in the 4'(*E*)-Methyl Group

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Summary Structural revisions are made to products formed when (—)-rotenone is treated with boron tribromide; stereospecific labelling of the 4' (*E*) methyl of (—)-rotenonic acid, a biosynthetic precursor of rotenone, can be achieved by treating product (4) with cyano-borodeuteride in hexamethylphosphorotriamide.

It has recently been reported that reaction of natural (6a*S*,12a*S*,5'*R*)-(—)-rotenone (1) with 1 mol. equiv. of BBr_3 gives the 1',5'-*seco*-bromide (2), whilst with 2 mol. equiv. of BBr_3 gives (3).^{1,2} Treatment of (2) with HCO_3^- provides the only method available for making (5'*S*)-rotenone, which is formed along with the (5'*R*)-diastereoisomer. However, structures (2) and (3) appeared at



variance with the n.m.r. data given¹ and the problem was re-examined. Treatment of rotenone with 1 mol. equiv. of BBr_3 in CH_2Cl_2 for 2 min at -5 to -10°C gave the 1',5'-*seco*-bromide, m.p. 152 – 154°C , which showed, along with other expected resonances, δ 3.35 (2H, d, 1'-H), 5.58 (1H, t,

2'-vinyl), and 3.87 (2H, s, 4'- CH_2) in the ^1H n.m.r. spectrum. In the ^{13}C n.m.r. spectrum there were resonances at δ 41.8 (t, C-4'), 22.3 (t, C-1'), and 14.7 (q, C-5'); the olefinic carbons resonated at 127.2(2') and 132.4(3') p.p.m. The compound is thus (4) and the cyclisation is an $\text{S}_{\text{N}}2'$ type (7); similar cases are known.⁴

Compound (4) has provided a means by which (–)-rotenonic acid (8) can be stereospecifically labelled in one of the pair of 4'- and 5'-methyls; since (8) is a precursor of rotenone,⁵ this affords a tool for studying the stereochemistry of formation of the isopropenylated ring E. The 4'- and 5'-methyls of (–)-rotenonic acid are readily distinguished by ^{13}C n.m.r. spectroscopy, the 4' (E)- group resonating at δ 25.8, and the 5' (Z)- group at 17.8 p.p.m.⁶ Treatment of (4) with sodium cyanoborohydride in hexamethylphosphorotriamide (HMPT) effected displacement of the 4'-halogen without reduction of the 12-carbonyl giving rotenonic acid, m.p. and mixed m.p. 206°C . Using cyanoborodeuteride, a single deuterium was introduced giving (9), M^+ 397, m.p. 206 – 207°C . That the replacement involves the 4' (E) carbon, is shown by collapse of the carbon resonance at 25.7 towards a triplet form in the off-resonance spectrum, the resonance at 17.83 p.p.m. being unaffected. The geometry of the bromo-compound is thus (4) and the deuterio-compound is (9), making the 4'-(E) tritiated compound potentially available. The BBr_3 reaction involving ring E may be represented as in (10).

The product formed when (–)-rotenone is treated with 2 mol. equiv. of BBr_3 requires further revision. It is reported, on slender n.m.r. spectroscopic evidence, that the second mol equiv. of reagent demethylates the 3-methoxy-group giving (3), and then (11) on cyclisation.^{2,3} The 1-proton in rotenone (1) resonates at δ 6.68 and the 4-proton at 6.41. Acetylation of monodemethylated 5'-(R)-rotenone formed on HCO_3^- treatment of the bromo-compound shifts the 1-proton from 6.78 to 6.89 leaving the 4-proton little changed in position (6.40 \rightarrow 6.43). Similarly, when the acetate is 6a,12a-dehydrogenated, the 1-proton resonates at δ 8.52 and the 4-proton at 6.51 (corresponding values for 6a,12a-dehydrorotenone are 8.41 and 6.49). Structural revision of (11) to (12) and (3) to (5) is thus indicated. It also appears that monodemethylated rotenone formed as a metabolite,² or photochemically,³ requires similar structural revision as regards ring A.

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¹ T. Unai and I. Yamamoto, *Agric. and Biol. Chem. (Japan)*, 1973, **37**, 897.

² T. Unai, H.-M. Cheng, I. Yamamoto, and J. E. Casida, *Agric. and Biol. Chem. (Japan)*, 1973, **37**, 1937.

³ H. M. Cheng, I. Yamamoto, and J. E. Casida, *J. Agric. Food Chem.*, 1972, **20**, 850.

⁴ F. Bohlmann and H. Franke, *Chem. Ber.*, 1971, **104**, 3229; F. Bohlmann and U. Bühlmann, *ibid.*, 1972, **105**, 863.

⁵ L. Crombie, P. M. Dewick, and D. A. Whiting, *J.C.S. Perkin I*, 1973, 1285, and references cited there.

⁶ L. Crombie, G. Kilbee, and D. A. Whiting, *J.C.S. Perkin I*, 1975, 1497.