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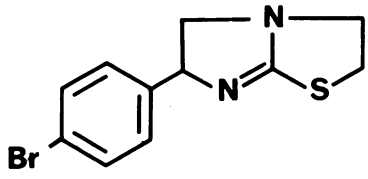
(-)-p-Bromotetramisole: a potent alkaline phosphatase inhibitor



p-**Bromotetramisole**

In the process of evaluating the biochemical effects of Tetramisole (*dl*-2,3,5,6-tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride), a broad-spectrum anthelmintic,[1] it was discovered that the compound was a potent inhibitor of alkaline phosphatase.[2] Consequently, similar studies were undertaken on the analogs of Tetramisole. Its levorotatory isomer, Levamisole (R12456, *l*-Tetramisole, *l*-2,3,5,6-tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride)[2-4] and R8231 {*dl*-6-(*m*-bromophenyl)-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole oxalate}[2-4] proved to be potent, stereospecific, noncompetitive inhibitors of alkaline phosphatase from various tissues, yet showed no inhibition of the intestinal isoenzyme. The *d*-isomers were completely inactive.

l-*p*-**Bromotetramisole** (R30402) has been found to be more potent than Levamisole as an inhibitor of alkaline phosphatase.[5-7] The inactive *d*-isomer, ***d*-*p*-bromotetramisole** (R30401), is useful as an internal control.

The organo- and stereospecificities of these alkaline phosphatase inhibitors have been demonstrated biochemically as well as cytochemically in a variety of tissues and species.[2-4,6-12] Specific phosphatase activities are not altered by these compounds.[4,7] Thus, this high degree of specificity allows the differentiation between "true" 5'-nucleotidase, Na-K-ATPase, Mg-ATPase or glucose-6-phosphatase and non-specific alkaline phosphatase, the latter being totally suppressed upon addition of the inhibitor.[4,7,13-18]

l-*p*-**Bromotetramisole** is reportedly more appropriate for the quantitative determination of the intestinal and placental isoenzymes in human serum than the commonly used L-phenylalanine.[6]

l-*p*-**Bromotetramisole** has several advantages over Levamisole and R8231:

1. potency - it is ten times as potent as Levamisole
2. stability - it is more stable in aqueous solution than R8231
3. the availability of both *levo*- and *dextro*-isomers.

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