Although the specific relevance of these structural differences is not understood fully at present, it seems logical to expect the substituents on C(2), C(3) and C(5) to influence the minimum-energy (preferred) orientations of the 4-phenyl and 4-OCOEt relative to the piperidine ring. As well as spatial requirements for the C(4) substituents, the vital factor for analgesic activity remains the accessibility of the lone pair on the N atom for interaction with the receptor as suggested by Belleau, Conway, Ahmed & Hardy (1974) and supported by comparison of the crystal structures of two isomers of the rigid 16,17-butanomorphinan-3-ol (Ahmed, 1981). The stereoelectronic nature of this interaction was discussed by Dimaio, Ahmed, Schiller & Belleau (1979).

The solid-state conformations of the isomers for (I), (II) and (III) are characterized by a piperidine ring in the chair form and an equatorial phenyl, except for the two crystalline forms of β-promedol alcohol, whose ester is the most active isomer of (II). There, the phenyl ring adopts an axial position while the piperidine ring remains in the chair form. The main features of an axial phenyl configuration are (1) the OH and the lone pair of the N atom are cis, (2) the phenyl ring has very little freedom of re-orientation through a twist about C(4)–C(10) (obvious from Fisher–Hirschfelder–Taylor atom model), and (3) the N···O separation is increased from 3.42–3.58 Å to 4.16–4.20 Å when the phenyl is equatorial. Further systematic comparisons with other analgesics are needed to ascertain which of the two conformations is the one actually adopted during interaction with the receptor.

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References


Book Reviews

Works intended for notice in this column should be sent direct to the Book-Review Editor (J. H. Robertson, School of Chemistry, University of Leeds, Leeds LS2 9JT, England). As far as practicable books will be reviewed in a country different from that of publication.

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Books Received
The following books have been received by the Editor. Brief and generally uncritical notices are given of works of marginal crystallographic interest; occasionally a book of fundamental interest is included under this heading because of difficulty in finding a suitable reviewer without great delay.

