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SYNTHESIS OF TWO TROPANE ALKALOIDS ISOLATED FROM KNIGHTIA DEPLANCHEI.

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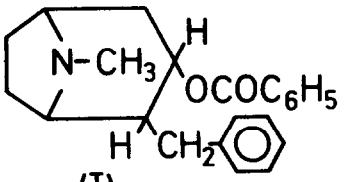
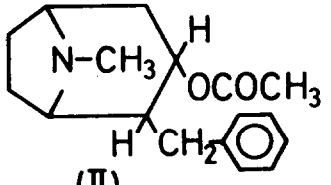
We have now synthesized the 2-benzyltropane alkaloids (I) and (II) recently isolated[1] from Knightia deplanchei Vieill. ex Brongn. et Gris (Proteaceae), and have thereby confirmed the gross structures proposed and obtained additional evidence for the existence of these alkaloids in racemic forms (dl-pairs).



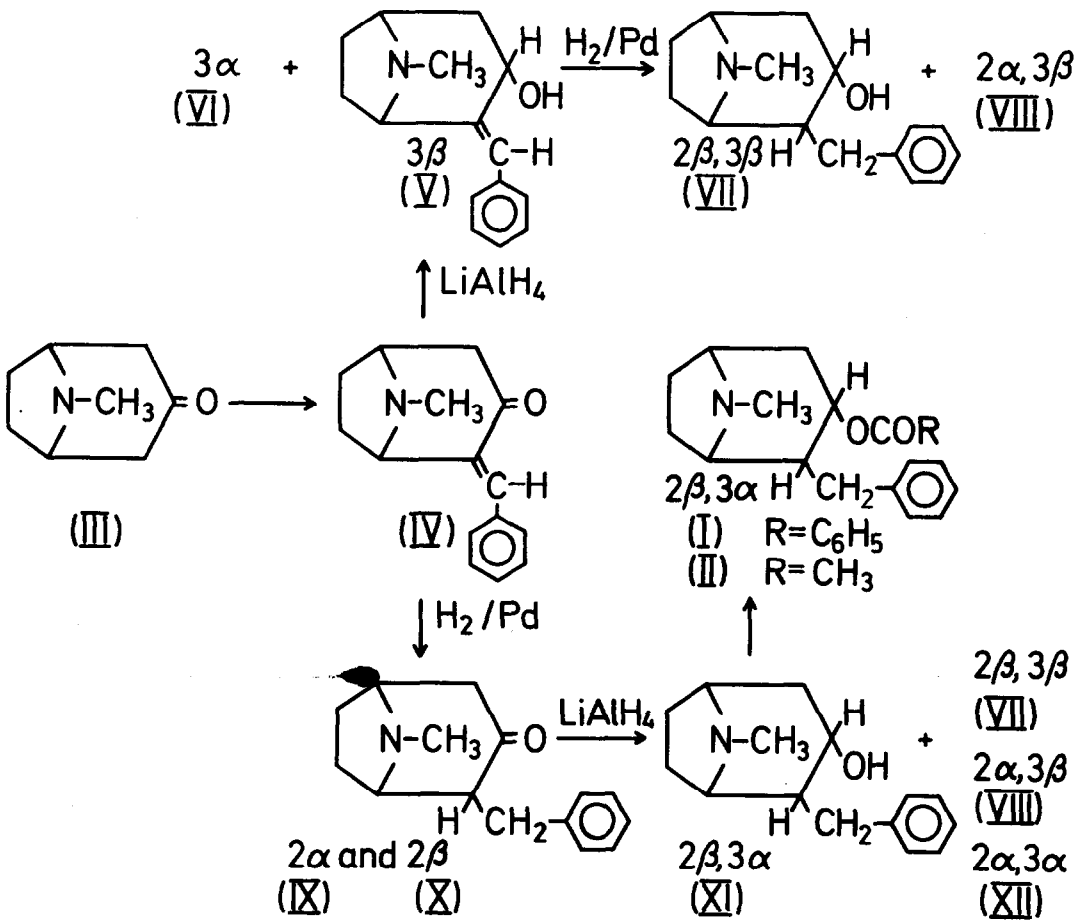
(I)



(II)

Despite negative indications in the literature[2,3,4] concerning the preparation of 2-benzylidenetropinone (cis and/or trans; for the nomenclature see ref. 4) by the base catalyzed condensation of tropinone (III) with benzaldehyde, this condensation reaction seemed so attractive to us as the first step for the preparation of the above-mentioned 2-benzyltropines (I and II) that we decided to examine the reaction in more detail. We found, in fact, that if the condensation reaction was executed under carefully controlled conditions and interrupted at an early stage, the desired trans-2-benzylidenetropinone (racemic)**(IV) could be obtained in reasonable yield (15%).

**All synthetic products described here are, of course, racemic.



Trans-2-benzylidenetropinone (IV) was reduced to the corresponding alcohols (V)(the major component, probably the 3β-isomer) and (VI)(the minor component, probably the 3α-isomer) with $LiAlH_4$. Owing to the presence of a β-aryl-α,β-unsaturated carbonyl system in trans-2-benzylidenetropinone (IV), we expected that the carbon-carbon double bond would be reduced, too.[5,6,7] However, it remained intact even after a relatively long reaction time.

Catalytic hydrogenation of trans-2-benzylidenetropanol (V) over palladium led to two 2-benzyltropanols, (VII)(the major component, probably the 2β,3β-isomer) and

(VIII)(the minor component, probably the 2α,3β-isomer), of which neither proved to be identical with the product obtained from alkaloids (I) and (II) by hydrolysis.[1]

However, when the trans-2-benzylidenetropinone (IV) was catalytically hydrogenated to 2-benzyltropinones (IX) and (X) and these, without separation, were reduced with $LiAlH_4$, a mixture of compounds (VII)(a major component, probably the 2β,3β-isomer), (VIII)(a minor component, probably the 2α,3β-isomer), (XI)(a major component, probably the 2β,3α-isomer), and (XII)(a minor component, probably the 2α,3α-isomer) was obtained. One of these (XI) proved to be identical (m.p., TLC, IR, NMR, and MS) to the product obtained by hydrolysis of the alkaloids (I) and (II).[1]

Transformation of 2-benzyltropanol (XI) to the corresponding hydrochloride followed by the esterification (with benzoyl- and acetylchloride) gave after normal work-up 2-benzyl-O-benzoyltropanol (I) and 2-benzyl-O-acetyltropanol (II)(both probably 2β,3α-isomers), which proved to be identical (TLC, IR, NMR, and MS) with the natural products (I) and (II), respectively.[1]

Trans-2-benzylidenetropinone (racemic)(IV). Oil. IR (film) ν C=O 1690 cm^{-1}, ν C=C 1610 cm^{-1}. NMR ($CDCl_3$) τ 2.52 (1H, s, olefinic), τ 2.68 (5H, apparent s, aromatic), τ 5.72 (1H, br m, H-1)(indicating the trans configuration, cf. ref. 4), τ 6.52 (1H, br m, H-5), and τ 7.62 (3H, s, $\rangle N-CH_3$). MS M^+ at m/e 227.

Trans-2-benzylidenetropanol (racemic)(V)(probably the 3β-isomer). White crystals. M.p. 130.5-131° (ether). IR (KBr) ν OH 3120 cm^{-1}, ν C=C 1600 cm^{-1}. NMR ($CDCl_3$) τ 2.70 (5H, narrow m, aromatic), τ 3.26 (1H, d, J=2Hz, olefinic), and τ 7.73 (3H, s, $\rangle N-CH_3$). MS M^+ at m/e 229.

2-Benzyltropanol (racemic)(VII)(probably the 2β,3β-isomer). White crystals. M.p. 100-101.5° (ether). IR (KBr) ν OH 3160 cm^{-1}, ν C=C 1608 cm^{-1}. NMR ($CDCl_3$) τ 2.78 (5H, apparent s, aromatic) and τ 7.83 (3H, s, $\rangle N-CH_3$). MS M^+ at m/e 231.

2-Benzyltropanol (racemic)(VIII)(probably the 2α,3β-isomer). MS M^+ at m/e 231.

2-Benzyltropanol (racemic)(XI)(probably the 2β,3α-isomer). White crystals. M.p. 123-124° (ether). For analytical data, see ref. 1.

2-Benzyltropanol (racemic)(XII)(probably the 2α,3α-isomer). MS M^+ at m/e 231.

2-Benzyl-O-benzoyltropanol (racemic)(I)(probably the 2β,3α-isomer). Oil. For analytical data, see ref. 1.

2-Benzyl-O-acetyltropanol (racemic)(II)(probably the 2β,3α-isomer). Oil. For analytical data, see ref. 1.

The stereochemical assignments presented for the compounds should be considered as purely tentative. A more detailed stereochemical study is in progress.

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