A TWO SYNTHON APPROACH TO $\Delta^{15,17,19}$-YOHIMBANE SKELETON VIA A N^5,N^{10}-METHYLENETETRAHYDROFOLATE MODEL. A FACILE ROUTE TO β-CARBOLINE ALKALOIDS.

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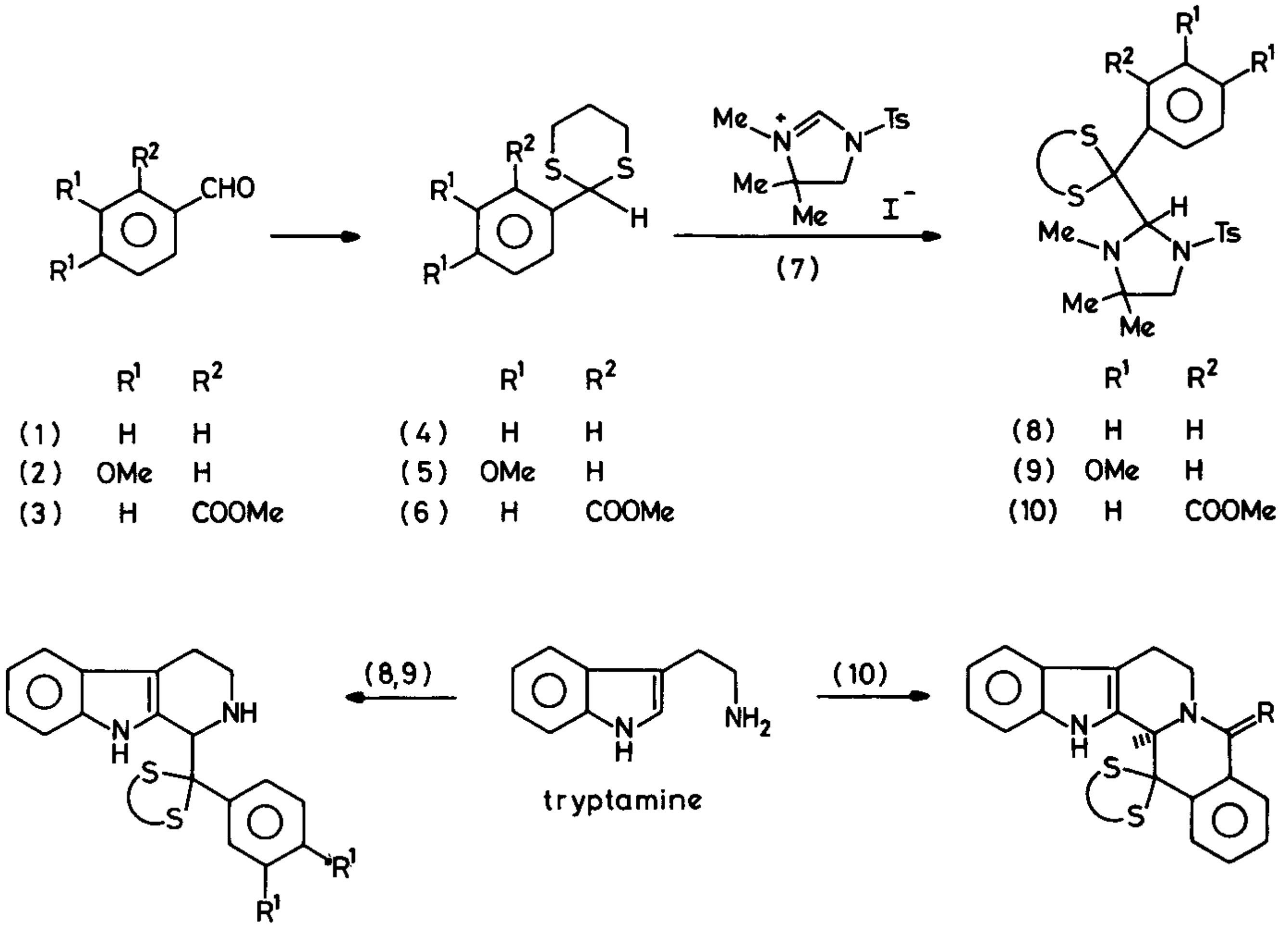
Abstract. 2[2-(1,5,5-Trimethyl-3-tosylimidazolidinyl)]-2-(2-methoxycarbonylphenyl)-1,3-dithiane (N^5,N^{10}-methylenetetrahydrofolate model 10) reacts in an acid catalyzed reaction with tryptamine to form the pentacyclic skeleton of $\Delta^{15,17,19}$-yohimbane in one practical step.

We have recently demonstrated that suitably substituted imidazolidine derivatives (N^5,N^{10}-methylenetetrahydrofolate models) are able to transfer carbon fragments to nucleophiles, via a mechanism which is analogous to that followed by the coenzyme (5,10-CH_2-H_4-folate)[1]. The reaction provides a principle method for synthesizing β-carboline and isoquinoline derivatives via the coupling of two readily accessible and potentially variable synthons. In this communication we report the synthesis of the pentacyclic system of $\Delta^{15,17,19}$-yohimbane, in one practical step, utilizing the two synthon approach.

For the preparation of the class of synthons required for the construction of the yohimbane skeleton, initially, model studies were carried out with the commercially available aldehydes (1) and (2). The latter were converted into their dithiane derivatives (4) and (5), respectively, and the corresponding lithium salts were allowed to react with the imidazolidinium salt (7) (n-BuLi, THF, -20°), whereupon the 5,10-CH_2-H_4-folate model synthons (8) and (9) were obtained (8, m.p. 174-175°, 82%, 9, foam, 70%). Reaction of these imidazolidines with tryptamine (1 eq., CH_3CN, reflux), in the presence of acetic acid, led to the facile formation of the β-carboline derivatives (11) and (12), respectively, in modest to good yields[2].

In order to apply the above mentioned approach to the synthesis of yohimbane derivatives, the synthon (10) was prepared via the sequence (3) ⟶ (6) LDA, -78° ⟶ (10). When a 1:1 mixture of (10) and tryptamine was refluxed in CH_3CN in the pre-



	R^1	R^2
(1)	H	H
(2)	OMe	H
(3)	H	COOMe

	R^1	R^2
(4)	H	H
(5)	OMe	H
(6)	H	COOMe

	R^1	R^2
(8)	H	H
(9)	OMe	H
(10)	H	COOMe

(11) $R^1 = H$
(12) $R^1 = OMe$

(13) $R = O$
(14) $R = H_2$

sence of acetic acid, the pentacyclic amide (13) crystallized out (m.p. 240-241°; 47%[2]; M^+ 392; 3420, 1645 cm^{-1}). Reduction of (13) with $LiAlH_4$ yielded the $\Delta^{15,17,19}$-yohimbane derivative (14) in which the characteristic Bohlmann bands (2750, 2780 cm^{-1}) attested to a trans junction of the C/D rings.

The precursor represented by (10), which can be conveniently varied by the choice *of the starting aldehyde, constitutes a general synthon for the preparation of* β-carboline and, in principle, of isoquinoline alkaloids. Studies directed to the syntheses of these classes of alkaloids via the "folic acid model approach" are actively in progress in this laboratory.

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Referrences.

* The structure of all new compounds was attested by their spectroanalytical data.

1. H. Bieräugel, R. Plemp, H.C. Hiemstra and U.K. Pandit, Heterocycles, 1979, **13**, 221.
2. No attempts have been made at this stage to optimize the yields, which we believe can be significantly improved.

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