RING TRANSFORMATIONS OF 1-AZA-DIBENZO[C,F]BICYCLO[3.3.1]NONA-3,6-DIENES

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In order to exploit pharmacologically active compounds, facile synthesis (via double cyclization) [*Tetrahedron Lett.*, 1307 (1978)] *and ring transformations of* 1-aza-dibenzo[c,f]bicyclo-[3.3.1]nona-3,6-dienes (1) optionally substituted at suitable positions have been developed in the following ways.

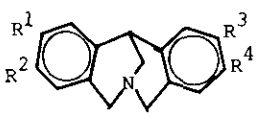
1) Reactions of the methiodides (2) of 1 with bases (t-BuOK).

In aprotic solvents (dioxane) 2 underwent Stevens rearrangement to give isopavine skeleton (4) (isopavine alkaloid (±)-amurensinine and (±)-reframine were derived [Heterocycles 9 1545 (1978)]), whereas in protic solvents (t-BuOH) dibenzazocine derivatives (5) were provided via Hofmann elimination. Key intermediates (5) were converted into dibenzotropanes (7) via dibenzopyrrolizine derivatives (6) by transannular reaction (with AcOH) followed by Stevens rearrangement (t-BuOK in dioxane). Furthermore, synthesis of a typical pavine alkaloid (±)-argemonine (8) from 5 (R^1=R^2=R^3=R^4=OMe) was accomplished in high overall yield [Chem. Commun., 1113 (1982)].

2) Reactions of the N-oxides (3) of 1.

a) Aziridine forming reaction —— Treatment of 3 with n-BuLi in ether produced a novel ring system (9) [Chem. Commun. 408 (1982)]. The mechanism on the formation of 9 will also be presented.

b) Regiocontrolled Polonovski-type reaction —— Reaction of 3 with t-BuOK in t-BuOH followed by treatment of ClCOOEt/aq. Na_2CO_3 was found to afford 4-(o-formylphenyl)-tetrahydroisoquinolines. Reactions of unsymmetrical 3 (R^1=OMe, R^2=R^3=R^4=H) with several Polonovski-type reagents have been examined in details and we found that the variable E_2 transition state theory could be applied to the reaction. By employing the methodology as a key step, natural alkaloid (-)-cherylline (10) was efficiently synthesized via optically resolved 1 (R^1=OMe, R^2=R^4=OBz, R^3=H).



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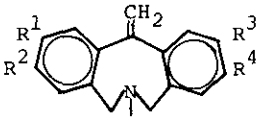
2 Methiodide

3 N-oxide



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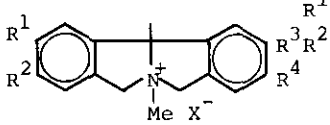

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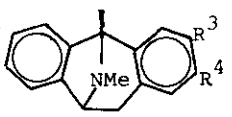

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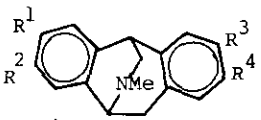

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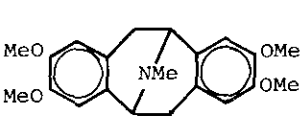

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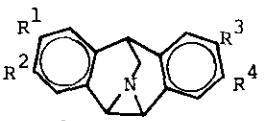

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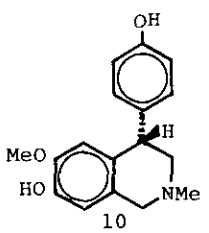

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