

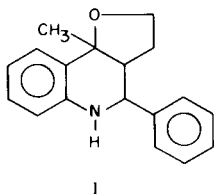
1,4-Cycloaddition Reactions. V. Preparation of
1,2,14*b*,14*c*-Tetrahydro-3*a*-methyl-3*a*H-furo[3',2':3,4]quino-
[1,2-*c*][1,2,3]benzotriazine *via* Povarov Precursors (1)

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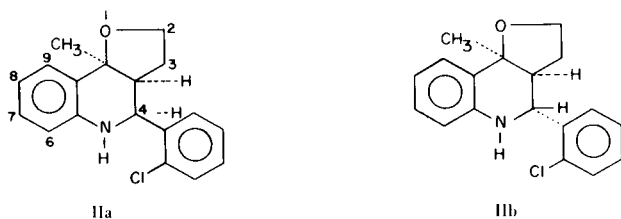
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Several years ago Povarov and coworkers pioneered the 1,4-cycloaddition of vinyl ethers to Schiff bases (2). Typical of the products obtained was 2,3,3*a*,4,5,9*b*-hexahydro-9*b*-methyl-4-phenylfuro[3,2-*c*]quinoline (1) (3).



Subsequently, the range of Schiff base used in the reaction was broadened to enable the facile preparation of many novel heterocyclic systems. Among the products obtained were dioxinofuroquinolines (4), dioxolofuroquinolines (4), furopyridoquinolines (5), furophenanthrolines (5), furopyrroloquinolines (5), cyclopentafuroquinolines (1), and furoindenoquinolines (1). In addition, the configuration of the isomers obtained was examined in detail. It was found, for example, that the reaction of *N*-(*o*-chlorobenzylidene)aniline with 5-methyl-2,3-dihydrofuran produced 2 products (II*a* and *b*) (6). The nmr spectrum showed that the doublet from the 4-proton of



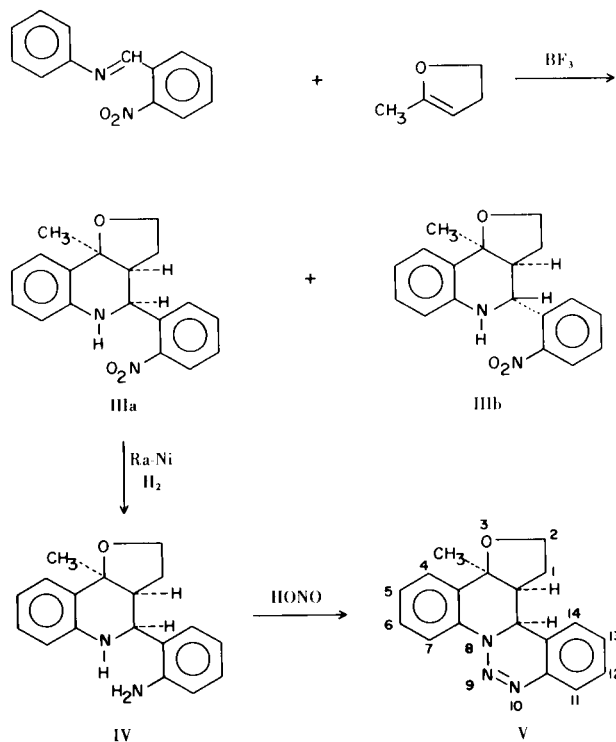
the *cis* isomer (II*a*) had a larger chemical shift (5.11 *vs.* 4.62) and a smaller *J*-value (2 *vs.* 8) than the signal from the *trans* isomer (II*b*). The position of the singlet from the 9*b*-methyl group was also a characteristic of each isomer (II*a*, 1.70; II*b*, 1.41) (6).

The present communication describes the synthesis of 1,2,14*b*,14*c*-tetrahydro-3*a*-methyl-3*a*H-furo[3',2':3,4]quino[1,2-*c*][1,2,3]benzotriazine (V) (Chart 1) utilizing

precursors derived *via* the Povarov reaction. This ring structure (V) is not listed in *Chemical Abstracts* or "The Ring Index" (7) and thus appears to be a unique heterocyclic system.

The condensation of *N*-(*o*-nitrobenzylidene)aniline and 2,3-dihydro-5-methylfuran proceeded smoothly (8). Examination of the nmr spectrum of the crude reaction mixture revealed doublets at 5.08 (*J* = 2) and 4.76 (*J* = 6) together with singlets at 1.68 and 1.21. It was assumed, therefore, that both of the isomers (III*a* and *b*) were present, and from the relative integration, in substantially equal amounts. Fortunately, crystallization gave a first crop containing essentially pure *cis* isomer (III*a*) showing a doublet at 5.19 (*J* = 2) and a singlet at 1.72.

CHART 1



Catalytic hydrogenation of IIIa over Raney nickel gave 4-(*o*-aminophenyl)-2,3,3a,4,5,9b-hexahydro-9b-methylfuro[3,2-*c*]quinoline (IV) in good yield which showed the expected doublet at 4.66 ($J = 2$) and singlet at 1.70. Treatment of IV with aqueous nitrous acid gave, according to thin layer chromatography, at least 5 products. Column chromatography, however, enabled the ready separation and isolation of the desired 1,2,14b,14c-tetrahydro-3a-methyl-3aH-furo[3',2':3,4]quino[1,2-*c*][1,2,3]benzotriazine (V) in low yield (8%). One attempt to increase the yield by using nitrosylsulfuric acid (9) was unsuccessful.

EXPERIMENTAL (10)

dl-2,3,3a,4,5,9b-Hexahydro-9b-methyl-4-(*o*-nitrophenyl)furo[3,2-*c*]quinoline (IIIa).

To a solution of 50 g. (0.22 mole) of *N*-(*o*-nitrobenzylidene)-aniline (11) in 500 ml. of benzene was added 1 ml. of boron trifluoride etherate followed by the dropwise addition of 19 g. (0.23 mole) of 2,3-dihydro-5-methylfuran in 50 ml. of benzene over 20 minutes. The temperature rose from 23 to 40°. After stirring for 4 hours, tlc (alumina, benzene) indicated complete conversion. The benzene was removed *in vacuo* to leave an oily residue (8). Crystallization from ethyl acetate gave 17.5 g. (26%) of the *cis* isomer; nmr: 5.19 (d, $J = 2$, H₄), 1.72 (s, CH₃).

Anal. Calcd. for C₁₈H₁₈N₂O₃: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.84; H, 6.09; N, 9.00.

dl-4-(*o*-Aminophenyl)-2,3,3a,4,5,9b-hexahydro-9b-methylfuro[3,2-*c*]quinoline (IV).

A solution of 17.5 g. (0.0565 mole) of *dl*-2,3,3a,4,5,9b-hexahydro-9b-methyl-4-(*o*-nitrophenyl)furo[3,2-*c*]quinoline (IIIa) in 100 ml. of methanol and 100 ml. of tetrahydrofuran was treated with 1 g. of Raney nickel and was hydrogenated in a Parr shaker under an initial pressure of 51.5 p.s.i.g. The mixture was filtered, and the filtrate was concentrated *in vacuo* to an oil which partially crystallized on standing. Recrystallization from ethanol gave 11.5 g. (73%), m.p. 145-149°; nmr: 4.66 (d, $J = 2$, H₄), 1.70 (s, CH₃).

Anal. Calcd. for C₁₈H₂₀N₂O: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.36; H, 7.30; N, 9.87.

dl-1,2,14b,14c-Tetrahydro-3a-methyl-3aH-furo[3',2':3,4]quino[1,2-*c*][1,2,3]benzotriazine (V).

To a cold slurry of 3.7 g. (0.013 mole) of *dl*-4-(*o*-aminophenyl)-2,3,3a,4,5,9b-hexahydro-9b-methylfuro[3,2-*c*]quinoline (IV) in 26 ml. of 1*N* hydrochloric acid was added dropwise a solution of 0.95 g. (0.014 mole) of sodium nitrite in 5 ml. of water. After stirring 5 minutes, the excess nitrite was destroyed

with a few drops of dilute, aqueous sulfamic acid. After stirring an additional 5 minutes in the cold, the precipitate was collected by filtration, washed with water, and dried to give 3.4 g. This was dissolved in benzene, placed on an alumina column (130 g.) and eluted with benzene followed by benzene containing successively larger proportions of ethyl acetate. Using tlc as the criterion, fractions 7-12 were combined and concentrated to an oil which crystallized on trituration with ethanol. Recrystallization from ethanol gave 0.3 g. (8%), m.p. 133-134°; nmr: 5.18 (d, $J = 2$ H_{14b}), 1.73 (s, CH₃); ir cm⁻¹: 1460 (s), 1100 (s), 1050 (s), 760 (s); uv λ max nm (methanol); 362 (ϵ , 10,900), 235 (ϵ , 15,600).

Anal. Calcd. for C₁₈H₁₇N₃O: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.16; H, 6.12; N, 14.38.

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