

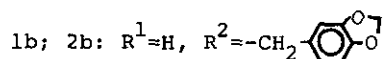
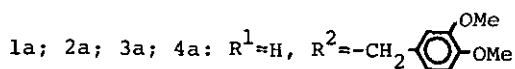
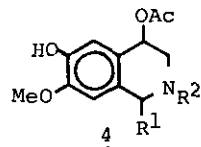
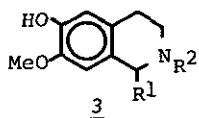
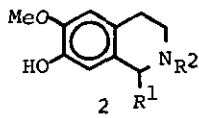
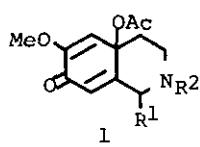
A NOVEL SYNTHESIS OF DIBENZO[*c,f*]-1-AZABICYCLO[3.3.1]NONANES[†]

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Abstract—Treatment of the *N*-benzylated *p*-quinol acetates (1a and 1b) with trifluoroacetic acid gave (±)-3-hydroxydibenzoazabicyclononanes (5a and 5c) in good yields. On the other hand, lead tetraacetate oxidation of 2-benzyl-6-hydroxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (3a) gave the *o*-quinol acetate (6), which rearranged into the 4-acetoxy-6-hydroxy derivative (4a) at room temperature. Acid treatment of the 4-acetate (4a) afforded a cyclization product (5e) having the same skeleton as that of 5a.

The *p*-quinol acetate (1), easily prepared from 7-hydroxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline (2) by lead tetraacetate (LTA) oxidation, is a key compound for the synthesis of isoquinoline alkaloids¹⁾, aporphine²⁾, homoaporphine, homoproaporphine, and homomorphinandienone.³⁾ On the other hand, LTA oxidation of 6-hydroxy-7-methoxy congener (3) gives the corresponding 4-acetoxy derivative (4)⁴⁾, which undergoes acid-catalysed cyclization to isopavine alkaloids.⁵⁾ Now we wish to report the synthesis of dibenzo[*c,f*]-1-azabicyclo[3.3.1]nonanes, through two routes via the *N*-benzylated *p*-quinol acetate (1) and 4-acetoxy derivative (4).



[†] Dedicated to Prof. T. Kametani on the occasion of his retirement.

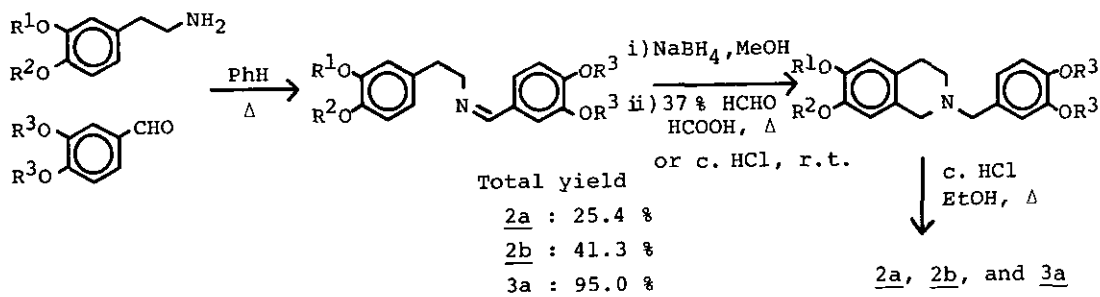
The starting phenols (2a,b and 3a) were prepared from benzaldehyde and β -phenethylamines according to Kametani's method⁶⁾ (condensation, reduction, Mannich's reaction, and debenzylation) as shown in Scheme I.

LTA (1.2 eq.) oxidation of 2a (100 mg) in acetic acid (AcOH) (1 ml) gave the *p*-quinol acetate (1a) [IR (cm^{-1}): 1735 (OAc), 1670, 1650, 1625 (dienone)] quantitatively, which was treated with trifluoroacetic acid (CF_3COOH) (1 ml) in methylene chloride (CH_2Cl_2) (10 ml) at room temperature for 1 hr to give ($\pm$)-3-hydroxy-2,9,10-trimethoxydibenzo[*c,f*]-1-azabicyclo[3.3.1]nonane (5a)⁷⁾, m.p. 213-215°, in 38% yield, which showed four singlets due to aromatic protons (δ 6.39, 6.41, 6.56, 6.58) on its nuclear magnetic resonance (NMR) spectrum and was methylated with diazomethane to give a tetramethyl ether (5b). NMR spectra of both tetramethyl ether (5b) and the authentic sample⁸⁾ were completely superimposable.

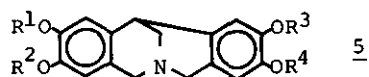
Similarly, oxidation and the subsequent acid treatment of 2b afforded ($\pm$)-3-hydroxy-2-methoxy-9,10-methylenedioxydibenzoazabicyclononane (5c), m.p. 203.5-205.5° (dec.), in 50% yield, the structure of which was confirmed by its conversion to the known methyl ether (5d).⁹⁾

Oxidation [LTA (1.2 eq.)] of 3a in CH_2Cl_2 and careful work-up¹⁰⁾ gave the oily *o*-quinol acetate (6) [IR (cm^{-1}): 1740 (OAc), 1685 (C=O); NMR (δ): 2.03 (OCOMe), 3.36 (aliph. OMe), 3.77 (2 x arom. OMe), 5.73, 5.79 (each 1H, olefin. H)], which was allowed to stand overnight to give a diastereomeric mixture of the 4-acetoxy derivatives (4a)¹⁰⁾ [IR (cm^{-1}): 3550 (OH), 1720 (OAc); NMR (δ): 1.95, 2.02 (3H, each s, OCOMe (1 : 1.3))] as an oil. Without purification, the 4-acetoxy derivatives (4a) were treated with CF_3COOH at room temperature for 1 hr to afford an amorphous ($\pm$)-2-hydroxy-3,9,10-trimethoxydibenzoazabicyclononane (5e) (HCl salt: m.p. 238-240°) in 80% yield from 3a. The structure of 5e was verified by comparison of its methyl ether with the authentic sample (5b)⁸⁾ in all respects.

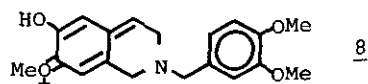
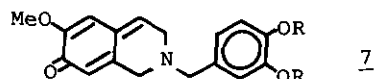
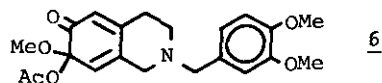
Thus a novel synthesis of ($\pm$)-dibenzo[*c,f*]-1-azabicyclo[3.3.1]nonanes (5) was accomplished from either 7- or 6-hydroxy-N-benzyltetrahydroisoquinoline (2a,b or 3a) via the intermediacy of either the *p*-quinol acetate (1a,b) or the 4-acetoxy derivatives (4a) presumably by the following reaction pathway; deacetoxylation of the former (1a,b) or the latter (4a) with acid would generate Michael-type acceptor, a *p*-quinone methide (7) or a cation (8), which would then immediately react together in a manner of intramolecular conjugate addition to form the products.



Scheme I



	R ¹	R ²	R ³	R ⁴
<u>5a</u>	Me	H	Me	Me
<u>5b</u>	Me	Me	Me	Me
<u>5c</u>	Me	H	-CH ₂ -	
<u>5d</u>	Me	Me	-CH ₂ -	
<u>5e</u>	H	Me	Me	Me



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7. All new compounds gave satisfactory analytical data. NMR and IR spectra were taken in CDCl_3 and CHCl_3 solution, respectively. Preparative t.l.c. was run on silica gel HF_{254} (Merck).
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