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NOVEL SYNTHESES OF DIBENZO[d,f]AZONINE AND DIBENZO-[e,g]AZECINE SYSTEMS

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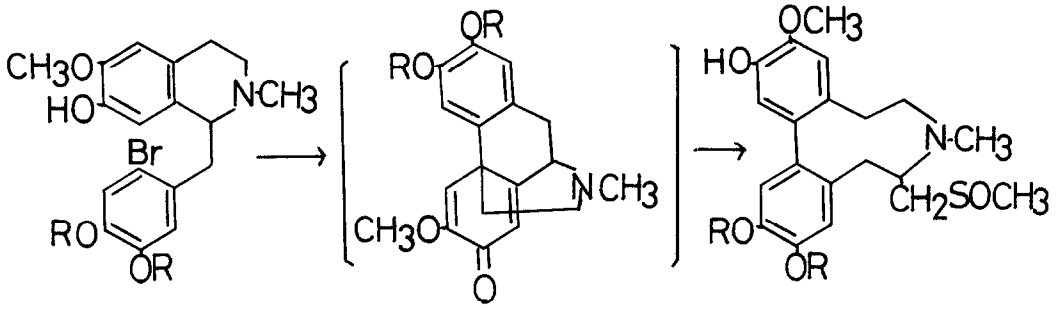
In the course of the investigation of reactions of 1-halogenobenzyl-1,2,3,4-tetrahydro-2-methylisoquinolines(1a,b) with sodium methylsulfinyl carbanion ($NaCH_2SOCH_3$)[1], it was found that the 8-substituted-dibenzo[d,f]azonines(3a,b) were yielded through the base catalyzed dienone-phenol rearrangement of morphinandienone intermediates(2a,b)[2]. We have successively studied the benzyne reaction of 1-halogenobenzyl-1,2,3,4-tetrahydro-2-methylisoquinoline(4) and 1-halogenophenethyl-1,2,3,4-tetrahydro-2-methylisoquinoline(5) using sodium methylsulfinyl carbanion in the expectation that the cyclohexadienone systems(6 and 7), formed as an intermediate, would be converted to the 8-substituted-dibenzo[d,f]azonine derivative(8) and dibenzo[e,g]azecine system (12), respectively, in the presence of sodium methylsulfinyl carbanion. Herein we wish to report an interesting ring transformation.

First, the reaction of 1-(2-bromo-4,5-dimethoxybenzyl)-1,2,3,4-tetrahydro-6-hydroxy-7-methoxy-2-methylisoquinoline(4) with sodium methylsulfinyl carbanion in dimethyl sulfoxide was investigated. The crude product was chromatographed on silicagel and the elution with 2 % methanol-chloroform afforded (8) as colorless needles, mp 184-186°(from methanol-ether). The structural formula, $C_{22}H_{29}NO_5S$ was determined by microanalysis and mass spectrum (M^+, m/e 419). Reductive deoxygenation of (8) with amalgamated zinc gave the methyl sulfide

derivativ(9) as colorless needles, mp 129-131°(from ether). S-methyl and N-methyl signals were observed at 2.08 and 2.55 ppm, respectively, in its NMR ($CDCl_3$) spectrum[3]. Further desulfurization of (9) with Raney Ni afforded the desired 8-methyldibenzo[d,f]azonine derivative(11) as colorless needles, mp 121-122°(from ether). Calcd. for $C_{21}H_{27}NO_4$: C,70.56; H,7.61; N,3.92. Found: C,70.22; H,7.72; N,3.62. Mass spectrum m/e 357 (M^+). A methyl signal due to C_8-methyl was observed at 1.47 ppm as doublet(J=7 Hz) and N-methyl signal resonated at 2.58 ppm in its NMR($CDCl_3$) spectrum. Four aromatic signals appeared at 6.62, 6.67, 6.70 and 6.78 ppm as singlets, respectively. Thus the product from the reaction of (4) with sodium methylsulfinyl carbanion was assigned to be the 8-substituted-dibenzo[d,f]azonine derivative(8). Oxidation of (8) with 30 % hydrogene peroxide afforded the methyl sulfone derivative(10)[4], mp 178-179°(from methanol). Its NMR($CDCl_3$) spectrum showed two methyl signals resonated at 2.03 and 2.45 ppm attributable to SO_2-methyl and N-methyl, respectively.

Secondly, this ring transformation reaction was applied to the 1-halogenophenethylisoquinoline(5). The isoquinoline(5) was treated with sodium methylsulfinyl carbanion to give (12), mp 239-241°(from ether). The molecular formula, $C_{23}H_{31}NO_5S$, was determined by microanalysis and mass spectrum (M^+, m/e 433). Reductive deoxygenation of (12) with amalgamated zinc yielded the methyl sulfide derivative(13), mp 155-155.5°(from methanol-ether). Its NMR ($CDCl_3$) revealed two methyl signals at 1.76 and 2.40 ppm attributable to S-methyl and N-methyl, respectively, as expected. Four aromatic protons resonated at 6.65, 6.78, 6.80 and 6.87 ppm as singlets, respectively. Desulfurization of (13) with Raney Ni in ethanol gave the 8-methyldibenzo[e,g]azecine derivative(14), mp 174-175°(from ether). Its NMR($CDCl_3$) showed a doublet (J=10 Hz) at 1.18 ppm due to C_8-methyl. N-methyl signal resonated at 2.40 ppm as singlet. Therefore, the product from the benzyne reaction of (5) with sodium methylsulfinyl carbanion was assigned to be the dibenzo[e,g]azecine derivative(12).

Thus sodium methylsulfinyl carbanion was found to be an excellent reagent for the ring expansion of 1-halogenobenzyl-1,2,3,4-tetrahydro-2-methyliso-



(1a) R=CH_3

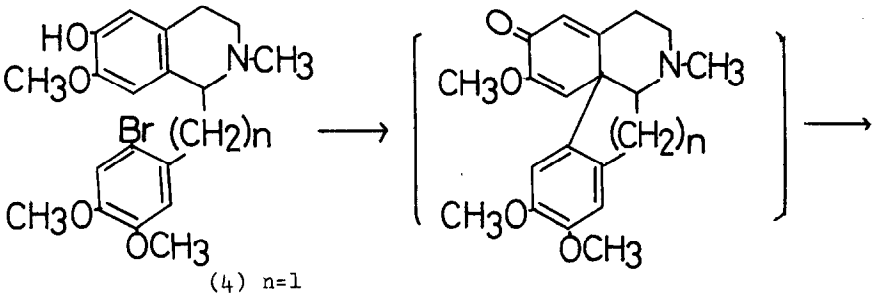
(1b) R=$-CH_2-$

(2a) R=CH_3

(2b) R=$-CH_2-$

(3a) R=CH_3

(3b) R=$-CH_2-$

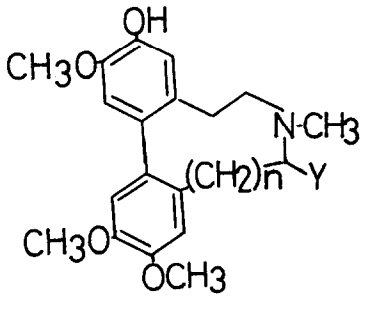


(4) n=1

(5) n=2

(6) n=1

(7) n=2



(8) n=1 Y=CH_2SOCH_3

(9) n=1 Y=CH_2SCH_3

(10) n=1 Y=$CH_2SO_2CH_3$

(11) n=1 Y=CH_3

(12) n=2 Y=CH_2SOCH_3

(13) n=2 Y=CH_2SCH_3

(14) n=2 Y=CH_3

quinolines and 1-halogenophenethyl analogues possesing a hydroxyl group at the 6-position.

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2. S. Kano, T. Ogawa, T. Yokomatsu, E. Komiyama and S. Shibuya, in preparation.
3. Nuclear magnetic resonances (NMR)($CDCl_3$) were taken with Varian T-60 spctrometer using TMS as a standard.
4. Microanalysis and mass spectrum (M^+, m/e 435) also supported this structure.