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A NOVEL SYNTHESIS OF HASUBANAN SKELETON

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Conversion of morphinan skeleton to hasubana[1] and synthesis of hasubanan-type alkaloids from β-tetralone derivatives[2] have been reported by several workers. In the course of our investigation on the synthesis of homomorphinans[3], we found a novel synthesis of hasubanan skeleton.

Treatment of 4a-(2-aminoethyl)-6-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene (1a)[4] with HCHO in HCO_2H (or in CH_3CO_2H)[*1] afforded an olefinic compound 2a (an oil of bp 150-160° (0.07 mmHg)), $C_{18}H_{23}NO$, N.W. 269 (mass spectrum[*2]: M^+ 269), in 90% yield.

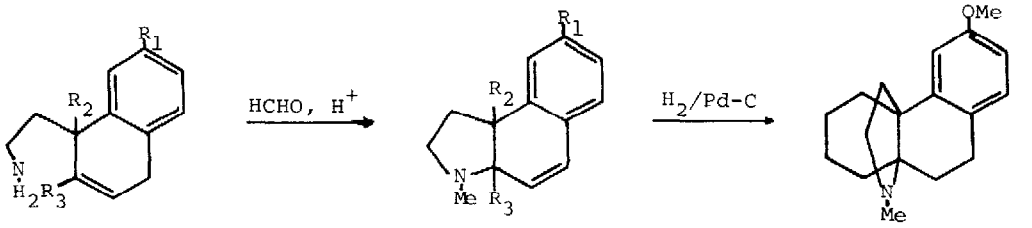
UV (λ_{max}^{EtOH} 215 nm (log ε: 4.36), 273 nm (log ε: 4.12)), NMR[*2] (δ 2.30 (s, 3H, NMe), 3.80 (s, 3H, OMe), 5.73; 6.42 (AB-type q, J = 10.0 Hz, 2H, olefinic H), 6.63 (double d, J = 2.5 Hz, J' = 8.0 Hz, 1H); 6.95 (d, J = 2.5 Hz, 1H); 7.02 (d, J = 8.0 Hz, 1H) three aromatic protons) and mass spectra (m/e 169 (M^+), 226 (M-43), 215 (M-54), 214 (M-55), 213 (M-56), 212 (M-57)), and elemental analysis of the picrate, mp 181.5-185° (from MeOH) (Anal. Calcd. for $C_{18}H_{23}NO \cdot C_6H_3N_3O_7$: C, 57.83; H, 5.26; N, 11.24. Found: C, 57.69; H, 5.37; N, 10.99.), suggested the compound 2a to be dl-9,10-dehydro-3-methoxy-N-methylhasubanan. Catalytic hydrogenation of 2a over Pd/C in MeOH-HCl gave dl-3-methoxy-N-methyhasubanan 3 as a colorless oil of bp 145-150° (0.06 mmHg), which was characterized as its picrate, mp 194-198° (from MeOH) (Anal. Calcd. for $C_{18}H_{25}NO \cdot C_6H_3N_3O_7$: C, 57.59; H, 5.64; N, 11.20 Found: C, 57.52; H, 5.63; N, 11.10.).

The racemic compound 3 and 3-methoxy-N-methylhasubanan[1c] derived from naturally occuring thebaine were identical in terms of their IR spectra (in $CHCl_3$).

Similarly, reactions of 1,2-dimethyl-1-(2-aminoethyl)-7-methoxy- (1b)[*3] and 1,2-dimethyl-1-(aminoethyl)-1,4-dihydronaphthalene (1c)[*3] with HCHO in HCO_2H (or in CH_3CO_2H)[*1] gave the corresponding benz[e]indole compounds 2b and 2c, respectively.

2b: bp 150-155° (0.25 mmHg); $C_{16}H_{21}NO$, M.W. 243 (mass spectrum M^+: 243); UV λ_{max}^{EtOH} 214.5 nm (log ε: 4.43), 271.5 nm (log ε: 4.21); NMR δ 0.96 (s, 3H, C-Me), 1.37 (s, 3H, C-Me), 2.39 (s, 3H, NMe), 3.80 (s, 3H, OMe), 5.75; 6.38 (AB-type q, J = 10.0 Hz, 2H, olefinic H), 6.65 (double d, J = 2.5 Hz, J' = 8.0 Hz, 1H); 6.96 (d, J = 2.5 Hz, 1H); 7.00 (d, J = 8.0 Hz, 1H) three aromatic protons: mass spectrum m/e 243 (M^+), 228 (M-15), 213 (M-30). Picrate: mp 170-175° (from MeOH) (Anal. Calcd. for $C_{16}H_{21}NO \cdot C_6H_3N_3O_7$: C, 55.93; H, 5.12; N, 11.86. Found: C, 56.23; H, 5.12; N, 11.48.).

2c: bp 110-120° (0.2 mmHg); $C_{15}H_{19}N$, M.W. 213 (mass spectrum M^+: 213); UV λ_{max}^{EtOH} 212 nm (log ε: 4.33), 217 nm (log ε: 4.33), 222 nm (shoulder)(log ε: 4.15), 259 nm (log ε: 3.86); NMR δ 0.94 (s, 3H, C-Me), 1.37 (s, 3H, C-Me), 3.37 (s, 3H, NMe), 5.83; 6.37 (AB-type q, J = 10.0 Hz, 2H, olefinic H); mass spectrum m/e 213 (M^+), 198 (M-15), 183 (M-30).



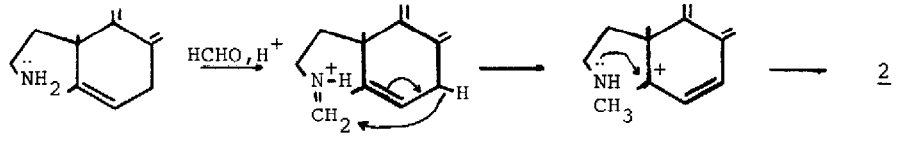
1a, 1b, 1c 2a, 2b, 2c 3

a: R_1 = OMe, R_2-R_3 = $-(CH_2)_4-$

b: R_1 = OMe, R_2 = R_3 = Me

c: R_1 = H, R_2 = R_3 = Me

This unusual intramolecular amination may resemble to Sommelet reaction[5] and is believed to involve hydride-ion transfer as follows: The conjugate acid of azomethine i initially formed would pull out the hydrogen activated by benzylic and allylic systems to form an intermediary carbonium ion ii which would cyclize to give the compound 2.



1 i ii

This interesting amination may have considerable synthetic importance. Applications to the similar allylic systems and further observations relative to the reaction mechanism will be presented in later papers.

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FOOTNOTES

*1 Reactions in CH_3CO_2H gave less yields.

*2 Mass spectra were recorded on a JEOL JMS-01SG mass spectrometer. All NMR spectra were taken on a JEOL PMX-60 spectrometer at 60 MHz in $CDCl_3$, using TMS as an internal standard.

*3 Compounds 1b and 1c were prepared from 2,2-dimethyl-7-methoxy-3,4-dihydro-1(2H)-naphthalenone and 2,2-dimethyl-3,4-dihydro-1(2H)-naphthalenone, respectively, by the method similar to that for compound 1a reported by Moncovic.[4]

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