ALTERNATIVE SYNTHESES OF 2,3-BENZAZOCIN-5-ONE DERIVATIVES VIA PYRROLO[1,2-a]INDOLES

Tetsuji Kametani, * Kimio Takahashi, Masataka Ihara, and Keiichiro Fukumoto
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

Transformations of 2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]indole (6) into hexahydro-2,3-benzazocine derivatives (6 and 2) using ethyl chloroformate or acetic anhydride were described.

The 2,3-benzazocin-5-one derivative 7 has been shown as a key intermediate in the total synthesis of mitomycins. We have recently reported the transformation of the pyrrolo[1,2-a]indole 3 into the 2,3-benzazocin-5-one 7 through 5. In this communication, we wish to report the alternative transformations of the pyrrolo[1,2-a]indole 7 to the 2,3-benzazocine derivatives (6, 7 and 10).

The reaction of the indoline 4, prepared from 7 with sodium borohydride reduction in acetic acid, with ethyl chloroformate in chloroform in the presence of sodium carbonate at room temperature for 8 hr gave 6 as a syrup [IR ν<sub>CHCl</sub>max 3 1690 cm<sup>-1</sup>; nmr δ...
Mitomycin A
(CCl₄) 1.16 (3H, t, J = 7 Hz, CH₂-CH₃), 2.16 (3H, s, ArCH₃), 3.84 (3H, s, OCH₃), 6.66 and 6.80 (each 1H, each s, ArH x 2); m/e 313, 311 (M⁺), 276 (M⁺-Cl), 202 (base peak) in a moderate yield.

On the other hand, heating the indoline 4 in acetic acid in the presence of acetic anhydride under reflux afforded, in a reasonable yield, the diacetate 7, mp 126 - 128°; ir νCHCl₃ 1725, 1640 cm⁻¹; nmr δ (CCl₄) 1.64 and 1.66 (each 1.5H, each s, NCOCH₃), 2.00 (3H, s, OOC=CH₂), 2.18 (3H, s, ArCH₃), 3.86 (3H, s, OCH₃), 6.60 and 6.80 (each 0.5H, each s, ArH), 6.90 (1H, s, ArH); m/e 305 (M⁺), 202 (base peak).

Hydrolysis of the O-acetyl group of this compound 7 with potassium carbonate in aqueous methanol afforded the alcohol 8, mp 167 - 168°; ir νCHCl₃ 1630 cm⁻¹; nmr δ (CCl₄) 1.64 and 1.66 (each 1.5H, each s, NCOCH₃), 2.14 (3H, s, ArCH₃), 3.80 (3H, s, OCH₃), 6.70 and 6.76 (each 0.5H, each s, ArH), 6.82 (1H, s, ArH); m/e 263 (M⁺).

The above nmr spectra of 7 and 8 would indicate the presence of two rotamers about the amide linkage in a ratio of ca 1:1.

The oxidation of 8 was carried out with chromium trioxide-pyridine complex in methylene chloride at room temperature to give the objective benzazocin-4-one 9 in a good yield, mp 148 - 149°; νCHCl₃ 1705 (C=O), 1650 cm⁻¹ (>NC=O); nmr δ (CDCl₃) 1.68 (3H, s, COCH₃), 2.18 (3H, s, ArCH₃), 3.66 (2H, s, ArCH₂CO), 3.84 (3H, s, OCH₃), 6.68 and 6.92 (each 1H, each s, ArH x 2); m/e 261 (M⁺).

Thus, two alternative routes to the benzazocin-4-one derivatives from 2,3-dihydro[1,2-a]indole have been developed.
REFERENCES


3. All new crystalline compounds gave satisfactory microanalyses and reasonable spectroscopic data.


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