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

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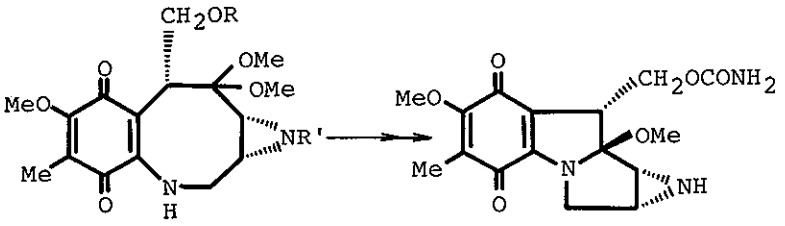
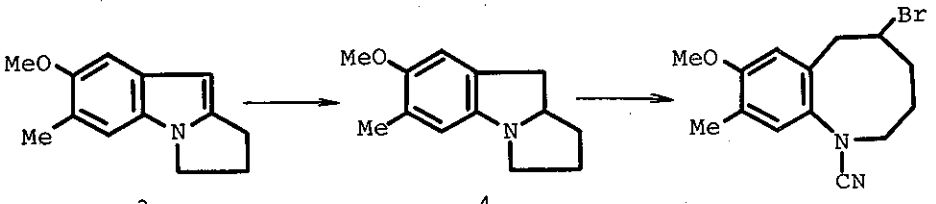
Transformations of 2,3,9,9a-tetrahydro-1H-pyrrolo-[1,2-a]indole (4) into hexahydro-2,3-benzazocine derivatives (6 and 7) using ethyl chloroformate or acetic anhydride were described.

The 2,3-benzazocin-5-one derivative 1 has been shown as a key intermediate in the total synthesis of mitomycins.[1] We have recently reported the transformation of the pyrrolo[1,2-a]indole 3 into the 2,3-benzazocin-5-one 9 through 5.[2] In this communication, we wish to report the alternative transformations of the pyrrolo[1,2-a]indole 3 to the 2,3-benzazocine derivatives (6, 7 and 10).

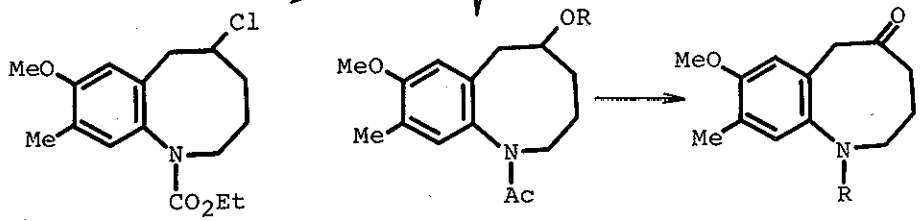
The reaction of the indoline 4, prepared from 3 with sodium borohydride reduction in acetic acid,[2] with ethyl chloroformate in chloroform in the presence of sodium carbonate at room temperature for 8 hr gave 6 as a syrup [ir $\nu_{max}^{CHCl_3}$ 1690 cm^{-1}; nmr δ



1 2 Mitomycin A



3 4 5



6 7 R=Ac 8 R=H 9 R=CN 10 R=Ac

(CCl_4) 1.16 (3H, t, $\underline{J}$ = 7 Hz, CH_2-$C\underline{H}_3$), 2.16 (3H, s, $ArCH_3$), 3.84 (3H, s, OCH_3), 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,[3] mp 126 - 128°; ir $\nu_{max}^{CHCl_3}$ 1725, 1640 cm^{-1}; nmr δ (CCl_4) 1.64 and 1.66 (each 1.5H, each s, $NCOCH_3$), 2.00 (3H, s, $OCOCH_3$), 2.18 (3H, s, $ArCH_3$), 3.86 (3H, s, OCH_3), 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,[3] mp 167 - 168°; ir $\nu_{max}^{CHCl_3}$ 1630 cm^{-1}; nmr δ (CCl_4) 1.64 and 1.66 (each 1.5H, each s, $NCOCH_3$), 2.14 (3H, s, $ArCH_3$), 3.80 (3H, s, OCH_3), 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.[4]

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 10[3] in a good yield, mp 148 - 149°; $\nu_{max}^{CHCl_3}$ 1705 (C=O), 1650 cm^{-1} (>NC=O); nmr δ ($CDCl_3$) 1.68 (3H, s, $COCH_3$), 2.18 (3H, s, $ArCH_3$), 3.66 (2H, s, $ArCH_2CO$), 3.84 (3H, s, OCH_3), 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

1. T. Fukuyama, F. Nakatsubo, A. J. Cocuzza, and Y. Kishi, Tetrahedron Letters, 1977, 4295 and references cited therein.

2. T. Kametani, K. Takahashi, M. Ihara, and K. Fukumoto, Heterocycles, 1977, 6, 1371; J. C. S. Perkin I, in the press.

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

4. C.f. M. Shamma and L. Töke, J. C. S. Chem. Comm., 1973, 740.

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