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SYNTHESIS AND X-RAY CRYSTAL STRUCTURE DETERMINATION OF
1,4-DIHYDROCYCLOPENT[b]INDOLES¹⁾

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Diethyl 1,4-dihydro-3- β -indolyl-4-methylcyclopent[b]indole-1,2-dicarboxylates (**2** and **5**) were synthesized and their structures were unambiguously established by the X-ray analysis of **5**.

KEYWORDS ——— pyrazolo[1,5-a]pyrimidine; triethyloxonium fluoro-borate; indole; N-methylindole; 1,4-dihydrocyclopent[b]indole; X-ray analysis

Recently, we reported the reaction of 6,7-diethoxycarbonylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (**1**) with a variety of nucleophiles, such as phenol, naphthol, aniline, enamine of cyclohexanone and their analogs, in the presence of boron trifluoride (BF₃)-etherate¹⁾ or triethyloxonium fluoroborate²⁾ (Et₃OBF₄) to give the respective addition products in a 1,4-fashion in the pyrimidine ring of **1**. Here we would like to report a synthesis and X-ray crystal structure determination of novel 1,4-dihydrocyclopent[b]indoles (**2** and **5**), which were prepared by reaction of **1** with indoles in the presence of excess Et₃OBF₄.

Cyclopent[b]indole itself was first isolated by Paul and Weise³⁾ as a hydrobromide salt in 1963, and many kinds of its 1,2,3,4-tetrahydro derivatives have been reported.⁴⁾ However, to our knowledge 1,4-dihydrocyclopent[b]indole has so far been unknown, probably because of the presence of an unstable cyclopentadiene moiety in its molecule.

Two equivalents of N-methylindole added to a mixture of **1** and Et₃OBF₄ in CH₂Cl₂ at room temperature furnished a 69.6% yield of **2** as orange needles, C₂₇H₂₆N₂O₄ [MS m/z : 442 (M⁺)], mp 171-173°C, IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹ : 1720 and 1690 (CO), ¹H NMR (DMSO-d₆) δ : 0.97 and 1.24 (each 3H, each t, J=7 Hz, 2 $\times$ CO₂CH₂CH₃), 3.44 and 3.91 (each 3H, each s, 2 $\times$ NCH₃), 3.80-4.35 (4H, m, 2 $\times$ CO₂CH₂CH₃), 4.84 (1H, s, CH, disappeared upon D₂O addition), 7.00-7.70 (8H, m, Ar-H), 7.79 [1H, s, C(2)-proton of indole ring], UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) : 369 (4.25), 260 (4.25), 218 (4.73). These analytical and spectral data clearly indicate lack of an aminopyrazole moiety in the molecule of **2**. These data show that **2** consists of two N-methylindoles and three carbons and one hydrogen as well as two CO₂C₂H₅ groups derived from the starting material. Treatment of **1** with N-methylindole in the presence of BF₃-etherate as a catalyst yielded **3**¹⁾, which, by methylation with dimethylsulfate and KOH in acetone, was converted quantitatively to **4**, mp 172-173°C. When this compound was then subjected to reaction with indole in the presence of Et₃OBF₄, it furnished an 8.0% yield of **5** as orange needles, C₂₆H₂₄N₂O₄ [MS m/z : 428 (M⁺)], mp 190-191°C, together with a complex mixture. This product exhibited spectroscopic data similar to those of **2**.

Thus, in order to obtain definitive evidence for the structure of $\underline{2}$ and $\underline{5}$, an X-ray crystallographic analysis of $\underline{5}$ was carried out.

Crystal data: monoclinic, space group $P2_1/n$, $a = 13.326(3) \text{ \AA}$, $b = 9.210(2) \text{ \AA}$, $c = 18.872(4) \text{ \AA}$, $\beta = 105.41(2)^\circ$, $V = 2232.9(9) \text{ \AA}^3$, $Z = 4$, $D_m = 1.267(1) \text{ g}\cdot\text{cm}^{-3}$, and $D_x = 1.274 \text{ g}\cdot\text{cm}^{-3}$. The structure was determined by the direct method (program MULTAN⁵) and refined by the block-diagonal least-squares method with anisotropic temperature factors for non-hydrogen atoms and isotropic ones for hydrogen atoms. The R-value for 3800 independent reflections is 0.071. The structure was unambiguously established as diethyl 1,4-dihydro-3- β -indolyl-4-methylcyclopent[b]indole-1,2-dicarboxylate ($\underline{5}$), whose stereoscopic view is presented in Fig. 1. Hence, the

Fig. 1

structure of $\underline{2}$ was determined to be diethyl 1,4-dihydro-4-methyl-3- β -N-methyl-indolylcyclopent[b]indole-1,2-dicarboxylate.

The transformation of $\underline{1}$ into $\underline{2}$ probably involves the initial formation of the adduct ($\underline{8}$). So the nucleophilic attack of the second N-methylindole at C(5)-position of $\underline{8}$ may form $\underline{9}$. Subsequent intramolecular cyclization leaving the amino-

Chart 2

pyrazole moiety followed by prototropy would ultimately yield **2** as shown in Chart 2.

It should be noted that although the C(1)-proton signal of **2** or **5** disappeared upon D₂O addition in DMSO-d₆, no exchange was observed in CDCl₃ in its ¹H NMR spectrum, respectively. In addition, treatment of **2** with KOH in EtOH afforded the unexpected 1-hydroxycyclopent[b]indole (**6**),⁶⁾ C₂₇H₂₆N₂O₅ [MS m/z : 458 (M⁺), mp 197-198°C]. Compound **5** gave **7**, C₂₆H₂₄N₂O₅ [MS m/z : 444 (M⁺), mp 173-174°C], under similar conditions.

The chemical reactivity of these 1,4-dihydrocyclopent[b]indoles is now under investigation.

REFERENCES AND NOTES

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- 6) Compound **6** : IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹ : 3340 (OH), 1720 and 1690 (CO); ¹H NMR (DMSO-d₆) δ : 0.88 and 1.06 (each 3H, each t, J=7 Hz, 2 × CO₂CH₂CH₃), 3.44 and 3.90 (each 3H, each s, 2 × NCH₃), 3.70-4.25 (4H, m, 2 × CO₂CH₂CH₃), 5.91 (1H, broad s, OH), 6.95-7.60 (8H, m, Ar-H), 7.78 [1H, s, C(2)-proton of indole ring].

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