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Communication

Oligomerization of N-Tosylindole with Aluminum Chloride

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The reactivity of *N*-tosylindole (4) in the presence of aluminum chloride was studied, and two types of oligomerization of 4 were observed. One type was condensation between both pyrrole parts (dimers 5 and 6 and trimer 7) and the other was between a pyrrole part and a benzene part of each indole nucleus (dimers 8 and 9).

Key words: indole polymerization; 3,3'-biindole; N-tosylindole

Although many indole alkaloids containing functional groups on the benzene part of the indole nucleus have been reported, introduction of the functional groups at specific positions was difficult, except in a few cases.¹⁾ We have developed novel methods²⁻¹⁰ for introducing various functional groups on the benzene part of such stabilized indoles as N-pivaloylindole and applied these to the total synthesis of teleocidin B^{11} and to an efficient synthesis of the mitomycin skeleton.¹²⁻¹⁴⁾ In a study of the chemical reactivity of N-pivaloylindole, we found novel dimerization of N-pivaloylindole in the presence of AlCl₃ to give 1a-c.¹⁵⁾ These compounds were completely different from oligomerization products 2 and 3^{16-19} of indole itself under acidic conditions. We report in this communication novel dimerization products of N-tosylindole (4).

The reactivity of *N*-tosylindole $(4)^{20}$ was studied by treating with AlCl₃ under various conditions, and two types of oligomerization of **4** were observed at low temperature. One of these was condensation between both pyrrole parts (dimers **5** and **6** and trimer **7**) and the other was between a pyrrole part and a benzene part of each indole nucleus (dimers **8** and **9**).



Fig. 1. Structures of the Polymers of N-Pivaloylindole $^{15)}$ and Indole. $^{18,19)}$

When the reaction was carried out with 1.0 eq. AlCl₃ in CH₂Cl₂ at 25°C for 25 min, the major product was trimer **7**, the tri-tosylamide of **3**, in a 71% yield (entry 1). It is considered that trimer **7** was formed by 1) partial coordination of **4** with AlCl₃ at the pyrrole part, 2) condensation between the electron-deficient tosylindole/AlCl₃ complex and electron-rich tosylindole, and 3) subsequent ring-opening by the same oligomerization mechanism as for the reaction of indole/HCl.¹⁷

When the reaction was carried out with 5.0 eq. AlCl₃ at 25°C (entry 2), unique 3-3' dimer **5** was generated as the major product, along with small amounts of similar dimers **8a–c** and **9a–c**. It is considered that the electron-withdrawing tosyl group made the reactivity of the pyrrole part considerably weake by the coordination of AlCl₃, this being an unexpected result. At low temperature (entries 3 and 4), the yields of **6** and **9a–c** were increased.

Since the structures of those products were very similar to each other, it was very difficult to isolate each component. However, we succeeded in their purification by utilizing silica gel open column chromatography and HPLC (ODS and silica gel).

N-Tosylindole **4** was stirred with 5.0 eq. AlCl₃ in CH_2Cl_2 at 25°C for 2 min. The reaction mixture was purified in a silica gel open column (80% CH_2Cl_2 in hexane). After evaporating the fractions containing **5**, **6**, **8** and **9**, pure dimer **5** (27% yield) was isolated by recrystallizing the residue in CH_3CN .

5: mp 222–223°C; ¹H-NMR δ (500 MHz, CDCl₃): 2.35 (3H, s), 2.41 (3H, s), 3.85 (1H, dd, J = 7, 11 Hz), 4.34 (1H, dd, J = 10, 11 Hz), 4.51 (1H, dd, J = 7, 10 Hz), 6.87 (1H, d, J = 8 Hz), 6.90 (1H, d, J = 8 Hz), 6.97 (1H, s), 6.99 (1H, br.t, J = 8 Hz), 7.02 (1H, br.t, J = 8 Hz), 7.18 (2H, br.d, J = 8 Hz), 7.22 (2H, br.d, J = 8 Hz), 7.27 (1H, t, J = 8 Hz), 7.30 (1H, br.t, J = 8 Hz), 7.61 (2H, d, J = 8 Hz), 7.68 (2H, d, J = 8 Hz), 7.78 (1H, d, J = 8 Hz), 7.93 (1H, d, J = 8 Hz); EI-MS m/z: 542 (M⁺).

In order to determine the structure of **6**, an authentic sample was prepared by tosylating indole dimer 2^{18} (NaH, TsCl in DMF, 31% isolated yield). Dimer **6** was identical with those derived from dimer **2**.

6: ¹H-NMR δ (500 MHz, CDCl₃): 2.31 (3H, s), 2.32 (3H, s), 2.95 (1H, dd, J = 3, 16 Hz), 3.23 (1H, dd,

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Scheme 1. Polymerization of N-Tosylindole in the Presence of Aluminum Chloride.



Scheme 2. Dimerization Mechanism for N-Tosylindole.



Scheme 3. Synthesis of Bi-indole 11.^{21–23)}

J = 10, 16 Hz), 5.53 (1H, dd, J = 3, 10 Hz), 7.02 (2H, d, J = 8 Hz), 7.07 (3H, m), 7.15 (1H, d, J = 8 Hz), 7.21 (2H, d, J = 8 Hz), 7.24 (1H, t, J = 8 Hz), 7.29 (1H, m), 7.45 (2H, d, J = 8 Hz), 7.58 (1H, s), 7.73 (1H, d, J = 8 Hz), 7.74 (2H, d, J = 8 Hz), 7.89 (1H, d, J = 8 Hz); EI-MS m/z: 542 (M⁺).

The structures of dimers **8a–c** were determined to be those of the dimers between the benzene part (6' > 4' > 5') and the 3-position by comparing with *N*pivaloyl indole dimers **1a–c**. Dimers **9a–c** were purified by HPLC, major component **9c** was isolated, and the structure **9c** was determined to be that of a novel 2-6' dimer between the benzene part (6'-position) and the 2position of the indole nucleus by a spectroscopic analysis.

9c: ¹H-NMR δ (500 MHz, d_6 -acetone): 2.31 (3H, s), 2.37 (3H, s), 2.91 (1H, m), 3.38 (1H, dd, J = 10, 16 Hz),

5.65 (1H, dd, J = 3, 10 Hz), 6.70 (1H, d, J = 3 Hz), 7.12 (1H, t, J = 8 Hz), 7.17 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.25 (4H, d, J = 8 Hz), 7.34 (1H, t, J = 8 Hz), 7.47 (1H, d, J = 8 Hz), 7.62 (1H, d, J = 3 Hz), 7.63 (2H, d, J = 8 Hz), 7.71 (2H, d, J = 8 Hz), 7.73 (1H, d, J = 8 Hz), 8.06 (1H, s); EI-MS m/z: 542 (M⁺).

The possible formation mechanism for dimer **5** is shown in Scheme 2: 1) 2 eq. AlCl₃ coordinates at both the tosyl group and 2-position of **4**, 2) electrophilic attack at the 3-position of AlCl₃ complex I to the 3-position of **10**, and 3) generation of **5**.

The structure of dimer **5** was determined to be that of the 3-3' dimer of *N*-tosylindole **4** from its spectroscopic data. Although the synthesis of 3-3' biindole **11** has been reported,^{21–23)} no synthetic route *via* the dimerization of indole has appeared in the literature.

Dimer 5 was oxidized with MnO₂ in CHCl₂CHCl₂ at

100°C for 90 min to give bi-indole derivative **10** in a 91% yield. Hydrolysis of **10** with KOH in dioxane at 100°C for 50 min afforded **11** in a 57% yield. The ¹H-NMR spectrum of **11** was identical with that reported.²³⁾

10: ¹H-NMR δ (500 MHz, CDCl₃): 2.35 (6H, s), 7.25 (4H, d, J = 8 Hz), 7.31 (2H, t, J = 8 Hz), 7.40 (2H, t, J = 8 Hz), 7.67 (2H, d, J = 8 Hz), 7.82 (4H, d, J = 8 Hz), 7.82 (2H, s), 8.07 (2H, d, J = 8 Hz); EI-MS m/z: 540 (M⁺).

The reactivity of *N*-tosylindole **4** in the presence of $AlCl_3$ might be important for a better understanding of indole chemistry. Further study of this reactivity is now in progress.

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