Direct Preparation of Rotaxane from Aminoalcohol: Selective *O*-Acylation of Aminoalcohol in the Presence of Trifluoromethanesulfonic Acid and Crown Ether

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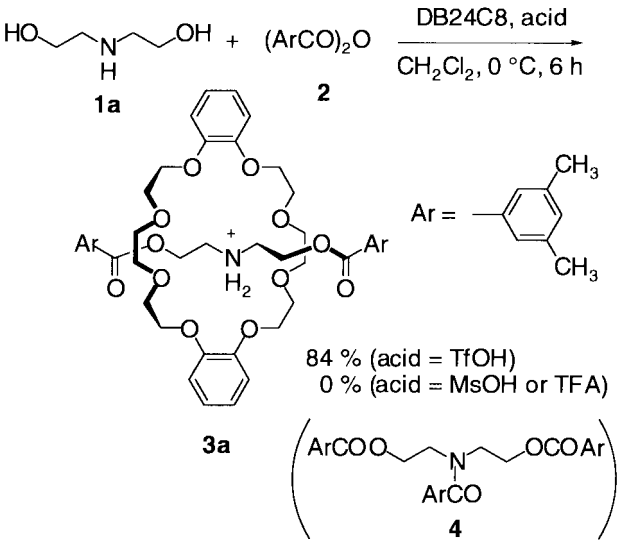
(Received April 2, 2001; CL-010297)

Selective *O*-acylation of aminoalcohols by a bulky acid anhydride in the presence of trifluoromethanesulfonic acid and dibenzo-24-crown-8 afforded [2]rotaxane in high yields. An acid halide could be used as an acylating reagent in the presence of silver trifluoromethanesulfonate.

End-capping of pseudorotaxane consisting of secondary ammonium salt and crown ether is one of the most easily accessible methods to rotaxanes.[1] Although various synthetic strategies to construct rotaxane structure have been proposed, they were carried out under neutral condition to prevent the neutralization of ammonium group. While basic condition is incompatible with the ammonium group,[2] acidic condition is acceptable.[3] When a strong acid-catalyzed end-capping reaction is employed, the corresponding amine can be used as a source of the axle unit instead of the ammonium salt because the ammonium salt can be generated by the acid in situ. Since water strongly inhibits hydrogen bonding interaction between ammonium salt and crown ether, strong acid-catalyzed method should be advantageous because it is unnecessary to use hygroscopic ammonium salt. In this paper, we wish to report a novel rotaxane synthesis from aminoalcohol and crown ether by selective *O*-acylation catalyzed by trifluoromethanesulfonic acid (TfOH).

To test the possibility of acid-catalyzed reaction for rotaxane synthesis, acid-catalyzed acylation of alcohol by acid anhydride was investigated. Selective *O*-acylation of diethanolamine (**1a**) by bulky acid anhydride **2** was carried out in the presence of slightly excess of strong acid and dibenzo-24-crown-8 (DB24C8) (Scheme 1). It should be noted that diethanolammonium salt is so hygroscopic that preparation of anhydrous salt, which is necessary for the rotaxane synthesis, is difficult even in the hydrophobic PF_6 salt form. The crude product was purified by preparative GPC, and corresponding [2]rotaxane **3a**[4] was obtained in 73% yield when TfOH was used as the acid. The rotaxane structure was established by ^1H and ^{13}C NMR, IR, FAB-MS, and the fact that repeated chromatography did not separate the components. By the optimization of the reaction conditions, **3a** was obtained in 84% yield when the reaction was carried out in dichloromethane at 0 °C for 6 h using 2 equivalents of DB24C8 and 1.5 equivalents of TfOH. In this protocol, crown ether is not only the component of the rotaxane, but also it protects ammonium group from acylating agent.[5] All chemicals used in this protocol are commercially available, except for **2** which was easily prepared from corresponding commercially available carboxylic acid.

The X-ray crystallographic analysis of **3a** confirmed the rotaxane structure (Figure 1).[6] Ammonium hydrogens showed hydrogen-bonding interaction with both crown ether and ester oxygen. Methylene group adjacent to ammonium group interacted with crown ether oxygen via CH···O hydrogen-bonding.



Scheme 1.

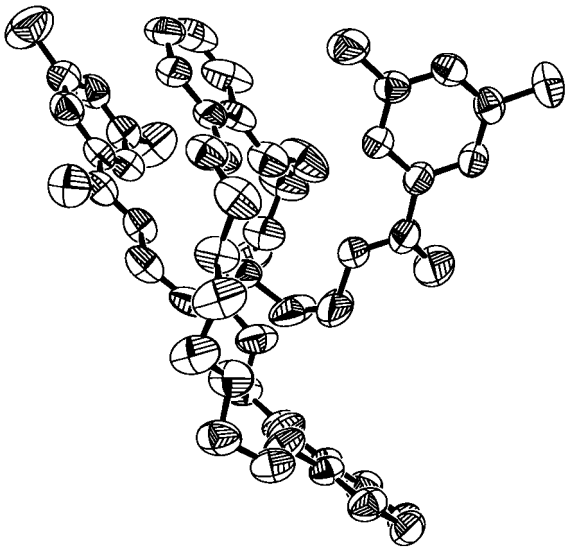
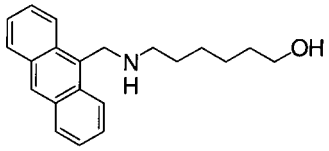
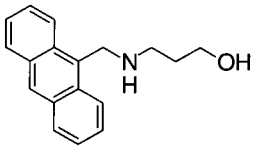
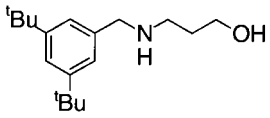
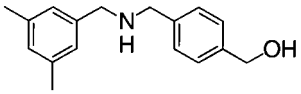
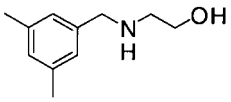


Figure 1. ORTEP drawing of **3a**. Hydrogens and TfO^- were omitted for clarity.

Further, there is π–π interaction between benzene ring in crown ether and 3,5-dimethylbenzoyl group. Stabilization of pseudorotaxane intermediate by these interactions accounts for the high yield of **3a**.

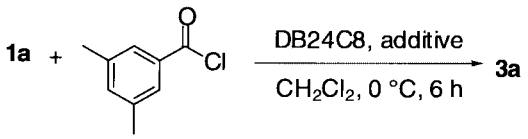
When trifluoroacetic acid (TFA) was used as the acid, no rotaxane but the trace amount of amide-ester **4** was obtained.

Table 1. Preparation of various rotaxanes[a]

Aminoalcohol	Rotaxane	Yield / %
	**3b**	94
	**3c**	96
	**3d**	86
	**3e**	85
	**3f**	92

[a]Reaction was carried out in dichloromethane (0.4 mol/L) at 0°C for 6 h in the presence of 2 equiv of DB24C8, 1.5 equiv of TfOH, and 1.5 equiv of **2**. The rotaxanes were isolated by preparative GPC.

The acidity of TFA was too low to protect the amino group by protonation. When methanesulfonic acid (MsOH) was used, no reaction occurred. Although the acidity of MsOH is high enough to protect the amino group, it is not sufficient to catalyze the esterification.



Additive	Yield / %
none	0
AgOTf (0.4 equiv)	19
AgOTf (2.2 equiv)	69
NaOTf (2.2 equiv)	0

Scheme 2.

Various [2]rotaxanes **3b–f** were prepared by this method. Every rotaxane was obtained in high yield. Especially, aminoalcohol bearing anthracene group gave the corresponding rotaxane in almost quantitative yields.[7] The yields are highest of those reported so far for the end-capping method.[2,8]

No rotaxane was obtained when acid halide was used as an acylation agent.[9] It is quite plausible that strong hydrogen-bonding interaction between chloride ion and ammonium group prevented the interaction between crown ether and ammonium group that is essential for the rotaxane formation. To remove chloride ion, silver triflate was added to the system, and rotaxane **3a** was obtained in 69% yield. Since more than one equivalent of silver ion was necessary to obtain **3a** in good yield, silver ion acted as an activator but not catalyst. Sodium triflate did not work as a chloride ion scavenger.

We acknowledge financial support by Grant-in-Aid for Scientific Research on Priority Areas (A) (No. 11133258) from the Ministry of Education, Science, Sports and Culture and grant from The Association for the Progress of New Chemistry.

References and Notes

1 a) N. Kihara and T. Takata, *Yuki Gosei Kagaku Kyokaishi*, **59**, 206 (2001). b) N. Kihara and T. Takata, *Rev. Heteroatom Chem.*, **22**, 197 (2001). c) S. J. Rowan and J. F. Stoddart, *Org. Lett.*, **1**, 1363 (1999).

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4 ^{1}H NMR (270 MHz, $CDCl_3$); δ 7.57 (s, 6H), 7.15 (s, 2H), 6.93–6.84 (m, 8H), 4.47 (t, J = 4.3 Hz, 4H), 4.22–4.12 (m, 8H), 3.96–3.80 (m, 12H), 3.70 (s, 8H), 2.21 (s, 12H) ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$); δ 166.0, 147.0, 137.8, 135.0, 128.5, 127.1, 121.8, 120.7 (q, J = 321 Hz), 112.7, 70.5, 70.2, 68.0, 60.1, 48.1, 20.9 ppm. IR (KBr); 3167, 3086, 2910, 1722, 1504, 1452, 1309, 1269, 1215, 1119, 1030, 958, 762, 752, 638 cm^{-1}. FAB-MS; 819.0 ([M+1]$^+$).

5 Protection of amino group as its salt form by coordination with 18-crown-6: T. W. Greene and P. G. M. Wuts, in "Protective Groups in Organic Synthesis," 3rd ed., Wiley, New York (1999), p. 596.

6 Crystal data for **3a**: $C_{47}H_{60}F_3NO_{15}S$, fw = 968.04, monoclinic, $P2_1/n$, a = 17.3738(4), b = 15.4176(3), c = 18.5597(5) Å, β = 96.6112(5)°, V = 4938.4(2) Å^3, Z = 4, μ(Mo Kα) = 1.4 cm^{-1}, D_{calc} = 1.302 g/cm^3, R = 0.078, R_w = 0.150 (668 variables on 7280, $I > 3\sigma(I)$), GOF = 1.05.

7 Y. Tachibana, N. Kihara, Y. Ohga, and T. Takata, *Chem. Lett.*, **2000**, 806.

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9 An analogous phenomenon was observed in the related system. See ref 2.