Tributylphosphine-catalyzed Acylation of Alcohol by Active Ester Directed toward Effective End-capping of Pseudorotaxane Consisting of Ammonium Group and Crown Ether

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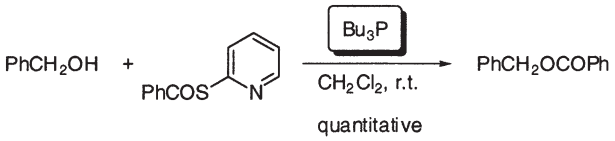
According to the results of a model study using benzyl alcohol, pseudorotaxane with terminal hydroxy group on the axle was acylated with *S*-2-pyridyl 3,5-dimethylthiobenzoate in the presence of tributylphosphine to produce rotaxane in 85% yield. Optically active [2]rotaxane and [3]rotaxane were readily synthesized by this method.

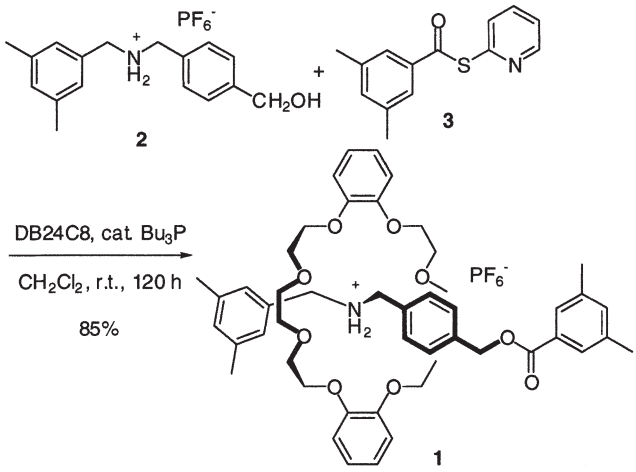
The end-capping of pseudorotaxane is one of the most easily accessible methods to prepare rotaxanes consisting of secondary ammonium salt and crown ether.[1,2] Although various synthesizing strategies have been proposed, limitations have arisen stemming from the fact that the reaction must be carried out without the neutralization of the ammonium group.[1] We have reported that the tributylphosphine-catalyzed acylation of the hydroxy group with acid anhydride is a highly effective and practical end-capping method.[1] However, this method cannot be applied to rotaxanes with functional groups that are incompatible with acid anhydride: for instance, the preparation of acid anhydride of amino acids is accompanied by racemization. Further, since acid anhydride has two reactive points, half of the anhydride is thrown away during the acylation. Thus, the acylation method is unsuited for the preparation of higher interlocked compounds such as [3]rotaxane. We found that these limitations could be overcome by the use of active ester as acylating agent. In this paper, we report that the acylation of alcohol with 2-pyridylthio ester takes place under neutral conditions and constitutes an effective means of producing rotaxanes that could not be prepared using the acid anhydride method.

While Busch reported the preparation of a rotaxane via the end-capping of amine with an active ester,[3] the end-capping of a hydroxy group poses great difficulty because amines, which are considered necessary for esterification with active esters, are incompatible with secondary ammonium salt-based rotaxane synthesis.[1] Thus, various catalysts for esterification under neutral conditions were examined in a model system. Reactions of benzyl alcohol with active esters of benzoic acid were carried out in dichloromethane at room temperature. Although most of the active esters, such as phenyl, *p*-nitrophenyl, succinimidoyl, and phenylthio ester, showed no or faint acylation activity without triethylamine, 2-pyridylthio ester quantitatively acylated benzylalcohol within 3 h in the presence of tributylphosphine as catalyst. TMSOTf, silver nitrate, triphenylphosphine, 1,2-bis(diphenylphosphino)ethane, triethyl phosphite, and triphenyl phosphite showed no catalytic activity. Thus, the combination of 2-pyridylthio ester and tributylphosphine appears suitable for the preparation of various interlocked compounds consisting of crown ether and secondary ammonium salt by acylative end-capping.



Scheme 1.

[2]Rotaxane **1** was prepared in 85% yield from ammonium salt **2** and 2-pyridylthio ester **3** in the presence of dibenzo-24-crown-8 (DB24C8) and a catalytic amount of tributylphosphine (Scheme 2).[4] The reaction proceeded more slowly than that of the model system, presumably because of steric hindrance of DB24C8. The NMR and IR spectra of **1** were identical to those reported elsewhere.[1] Since the yield by the active ester method is comparable with that by the acid anhydride method (90%), the method constitutes an effective alternate for the simple and practical preparation of rotaxanes.[5]

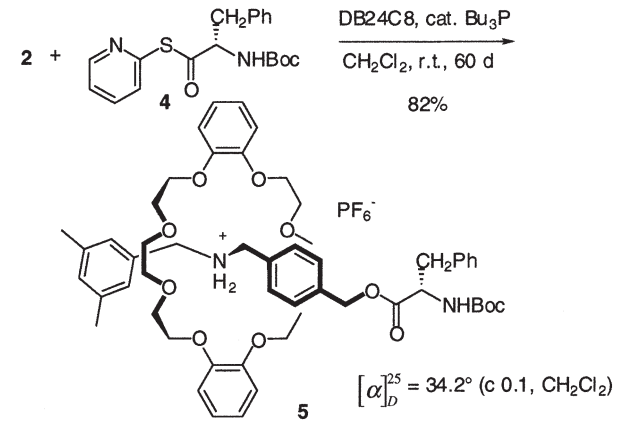


Scheme 2.

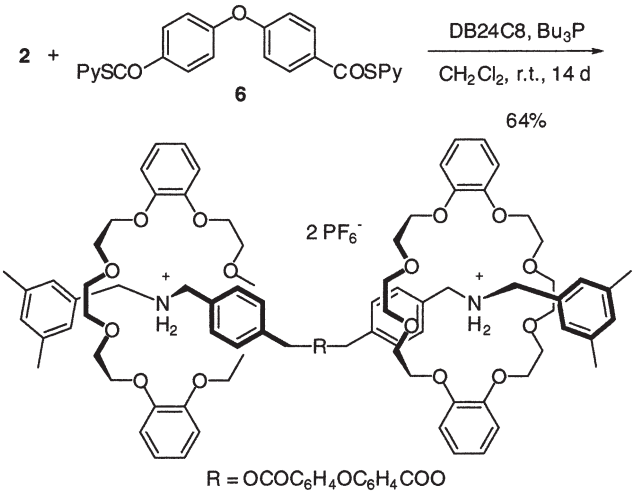
The effectiveness of the active ester method can be demonstrated by the synthesis of some functional rotaxanes and interlocked compounds having higher topology. First, **2** and 2-pyridylthio ester **4** derived from l-phenylalanine were reacted in the presence of DB24C8 and tributylphosphine to produce optically active [2]rotaxane **5** in a high yield[6] (Scheme 3).

Second, **2** was reacted with bifunctional active ester **6** in the presence of DB24C8 to generate [3]rotaxane **7** in a good yield[7] (Scheme 4). It should be pointed out that [3]rotaxane cannot be obtained by the acid anhydride method because acid anhydride has two equally reactive carbonyl groups.

In summary, we developed the tributylphosphine-catalyzed esterification of alcohol with 2-pyridylthio ester, and prepared higher functional rotaxanes using this novel acylation reaction. Further applications using these higherfunctional rotaxanes are under development.



Scheme 3.



Scheme 4.

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References and Notes

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4 Typical procedure: To a solution of 40 mg (0.10 mmol) of **2** and 47 mg (0.105 mmol) of DB24C8 in dichloromethane (0.2 mL) were added 36 mg (0.15 mmol)of active ester **3** and 3 μL (0.01 mmol) of tributylphosphine, and the reaction mixture was allowed to stand at room temperature for 5 days. The reaction mixture was purified by preparative HPLC (eluent: $CHCl_3$) to isolate 83 mg (85%) of **1** as a colorless solid.

5 Potentially basic **3** and 2-mercaptopyridine formed during the reaction may disturb pseudorotaxane formation from **2** and DB24C8. Thus, **3** and 2-mercaptopyridine were added to a $CDCl_3$ solution of **2** and DB24C8 to evaluate the effect of the additives. Since no change was observed in the ^{1}H-NMR spectra of the pseudorotaxane by the addition, neither **3** nor 2-mercaptopyrdine disturbs hydrogen-bonding between **2** and DB24C8 that stabilize the pseudorotaxane.

6 ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.58 (br, 2H), 7.4–7.1 (m, 12H), 6.9–6.7 (m, 8H), 5.10 (d, J = 13.2 Hz, 1H), 5.02 (br, 1H), 5.00 (d, J = 13.2 Hz, 1H), 4.7–4.6 (m, 3H), 4.5–4.4 (m, 2H), 4.2–4.0 (m, 8H), 3.8–3.7 (m, 8H), 3.47 (s, 8H), 3.1–3.0 (m, 2H), 2.15 (s, 6H), 1.39 (s, 9H); IR (KBr): 3151, 2927, 1743, 1714, 1506, 1254, 841, 557 cm^{-1}; FAB-MS (*m*-NBA): m/z 951.5 ([M-PF_6]$^+$); $[\alpha]_D^{25}$ 34.2° (c 0.1, CH_2Cl_2).

7 ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.09 (d, J = 8.5 Hz, 4H), 7.58 (br, 4H), 7.37 (d, J = 8.1 Hz, 4H), 7.26 (d, J = 8.1 Hz, 4H), 7.10 (d, J = 8.5 Hz, 4H), 6.9–6.7 (m, 22H), 5.26 (s, 4H), 4.6–4.5 (m, 4H), 4.5–4.4 (m, 4H), 4.2–4.0 (m, 16H), 3.9–3.7 (m, 16H), 3.46 (s, 16H), 2.14 (s, 12H); IR (KBr): 3273, 1718, 1595, 1504, 1248, 1109, 834, 557 cm^{-1}; FAB-MS (*m*-NBA): m/z 1630.7 ([M-2PF_6]$^+$).