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SYNTHESES OF UNSYMMETRICALLY N,N'-BIS(SUBSTITUTED)-4,13-DIAZA-18-CROWN-6-ETHER DERIVATIVES AS A NEW ELECTRON DONOR-SPACER-ACCEPTOR TRIAD

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Key Words: *inclusion molecule; unsymmetrically bis(substituted) diazacrown ether; donor-spacer-acceptor triad; intramolecular electron transfer; molecular device*

Abstract: *A simple and general synthetic strategy potentially applicable for the preparation of a wide variety of unsymmetrically N,N'-bis(substituted)-4,13-diaza-18-crown-6-ether derivatives was reported.*

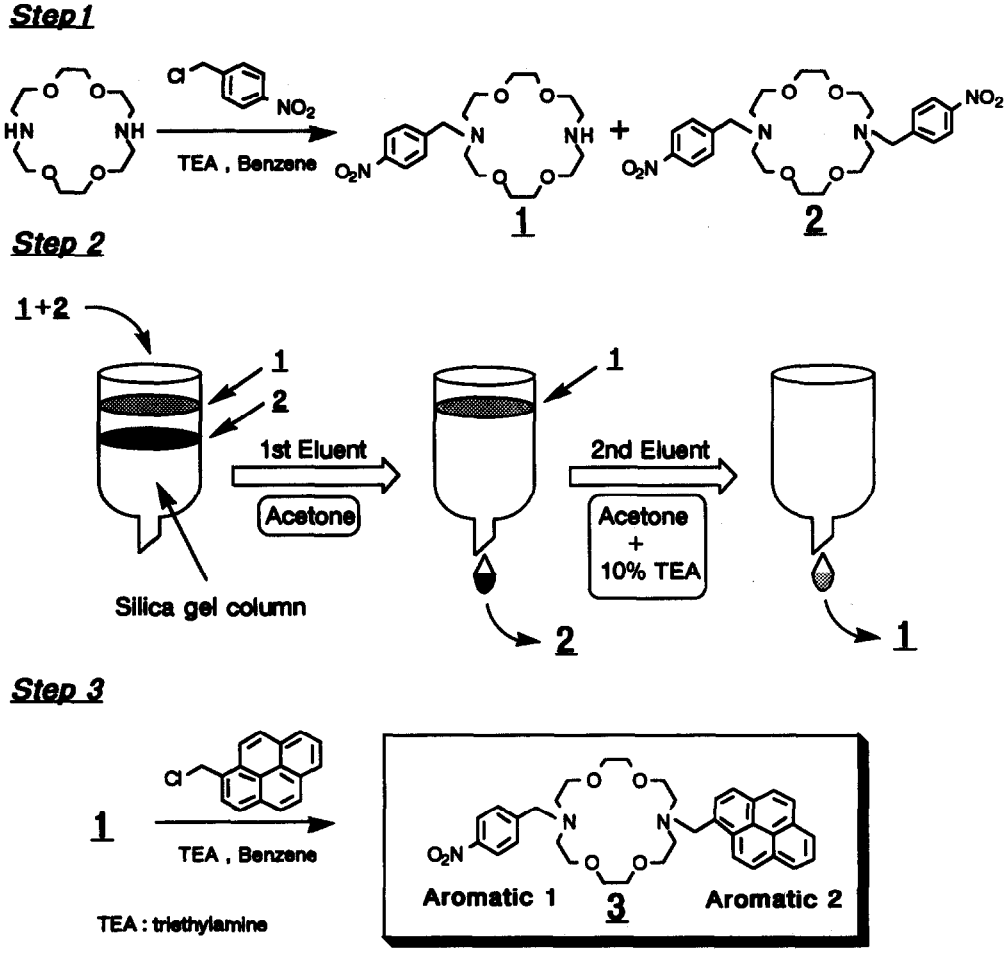
As a new approach to the manipulation of an intramolecular electron transfer dynamics, we have designed a new electron donor-spacer-acceptor triad[1] consisting of 4,13-diaza-18-crown-6-ether (diazacrown) as a spacer. The triad allows one to systematically control its intramolecular electron transfer rate through inclusion of various cations and their counterions which are to perturb the electronic state of the spacer. To synthesize such a triad, two secondary amines of the diazacrown should be substituted unsymmetrically by a donor and an acceptor groups. Symmetrically N, N'-bis(substituted) diazacrown derivatives which have side chains containing various kinds of functional groups are well known as bibracchial lariat ethers (BiBLEs)[2]. Additionally, the diazacrown has been used as one of the building blocks in supramolecules[3]. However, there have been a few works using unsymmetrically bis(substituted) diazacrown and their methods[4] for isolation were unsuited for our work. In this paper, we are reporting a simple and general strategy to prepare unsymmetrically bis(substituted) diazacrown derivatives.

Our synthetic procedure consists of three steps. **Step 1**: Substitution of aromatic molecule having chloromethyl- or carbonyl group to secondary amino groups of the diazacrown through tertiary amino- or amide linkage. **Step 2**: Separation of mono and bis(substituted) diazacrowns by column chromatography on silica gel. **Step 3**: Substitution of another aromatic molecule to the mono(substituted) diazacrown in the same manner as Step 1. The keystep on this method is the separation step (Step 2) which is easily accomplished by two kinds of eluting solvent system. With acetone as the first eluting solvent, the symmetrically bis(substituted) diazacrown was eluted while the mono(substituted) diazacrown remained uneluting on the silica gel. Using the solution of acetone/triethylamine (TEA, 9:1) as the second eluting solvent, the remaining mono(substituted) diazacrown was eluted. This solvents system was usable for syntheses of diazacrown derivatives listed in Table 1. This procedure may therefore be potentially applicable for the synthesis of an unsymmetrically bis(substituted) diazacrown which have various kinds of aromatic derivatives. A synthetic procedure is given below of N-(4-nitrobenzyl)-N'-(1-pyrenylmethyl) diazacrown (Scheme 1).

Step 1 : Preparation of mono(substituted) diazacrown derivative

Treatment of an unsubstituted diazacrown with equivalent of 4-nitrobenzylchloride[5,6] and excess TEA in benzene under reflux for overnight gave a mixture of mono(substituted) diazacrown **1** and bis(substituted) **2**.

Scheme 1



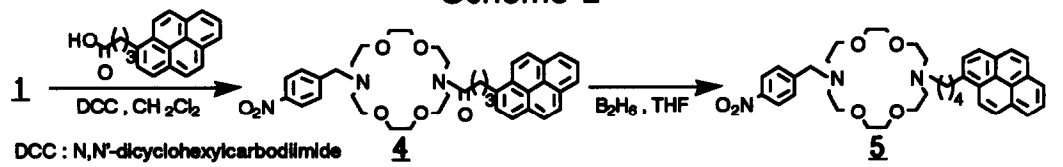
Step 2 : Separation of mono and bis(substituted) diazacrown derivatives

The separation of mono and bis(substituted) diazacrown derivatives was accomplished by short column chromatography (50ϕx70mm) on silica gel. Acetone as the first eluting solvent eluted the bis(substituted) 2 and unreacted 4-nitrobenzylchloride. The elution with acetone/TEA (9:1) as the second eluting solvent yielded the mono(substituted) 1 (47% yield). The bis(substituted) 2 was further purified by column chromatography (25ϕx350mm) on silica gel with acetone/benzene (5:5) as eluting solvent (13% yield). The mono(substituted) diazacrown 1 was used for next step without further purification.

Step 3 : Preparation of unsymmetrically bis(substituted) diazacrown derivative

Treatment of the mono(substituted) 1 with small excess of the 1-(chloromethyl)pyrene[7] in the same condition as mentioned above gave a desired unsymmetrically bis(substituted) diazacrown 3, and further purification was accomplished by column chromatography (25ϕx350mm) on silica gel with acetone/benzene (5:5) as eluting solvent (57% yield). The product was identified by ^{1}H-NMR analysis and elementary analysis[8].

Scheme 2



In the case of 1-pyrenylbutanoic acid[9] as a donor group having four carbon atoms (n=4) between pyrene moiety and nitrogen of diazacrown, another method was used for the condensation (Scheme 2). The mono(substituted) diazacrown 1 was reacted overnight with 1-pyrenylbutanoic acid in the presence of a small excess of N,N'-dicyclohexylcarbodiimide (DCC) in dichloromethane. After the product 4 was purified by column chromatography (25ϕx200mm) on silica gel with ethyl acetate, the amide linkage was reduced by diborane (B_2H_6) in tetrahydrofuran (THF) according to the conventional manner[4b]. The unsymmetrical N-4-nitrophenyl-N'-1-Pyrenylbutyldiazacrown 5 was purified by column chromatography (25ϕx350mm) on silica gel with methanol/ethyl acetate (9:1) as a eluting solution (53% yield). The product was identified by the ^{1}H-NMR analysis and elementary analysis[10].

Table 1. Syntheses of Unsymmetrically Bis(substituted) Diazacrown Derivatives[a)]

Aromatic 1	Linkage 1	Linkage 2	Aromatic 2	Yield (%)
phenyl	-CH_2-	-CH_2-	9-anthracenyl	28
phenyl	-CH_2-	-CH_2-	9-phenanthrenyl	43
phenyl	-CH_2-	-CH_2-	1-pyrenyl	64
phenyl	-CH_2-	-$(CH_2)_2$-	1-pyrenyl	11
phenyl	-CH_2-	-$(CH_2)_3$-	1-pyrenyl	42
phenyl	-CH_2-	-$(CH_2)_4$-	1-pyrenyl	21
phenyl	-CH_2(C=O)-	-(C=O)CH_2-	1-pyrenyl	32
4-nitrophenyl	-(C=O)-	-(C=O)CH_2-	2-naphthyl	34
4-nitrophenyl	-CH_2(C=O)-	-(C=O)CH_2-	2-naphthyl	39
4-nitrophenyl	-CH_2-	-CH_2-	9-anthracenyl	24
4-nitrophenyl	-CH_2-	-CH_2-	9-phenanthrenyl	59
4-nitrophenyl	-CH_2-	-CH_2-	1-pyrenyl	57
4-nitrophenyl	-CH_2-	-$(CH_2)_2$-	1-pyrenyl	61
4-nitrophenyl	-CH_2-	-$(CH_2)_3$-	1-pyrenyl	62
4-nitrophenyl	-CH_2-	-$(CH_2)_4$-	1-pyrenyl	53
4-nitrophenyl	-CH_2(C=O)-	-(C=O)CH_2-	1-pyrenyl	15
2,4-dinitrophenyl	-CH_2(C=O)-	-(C=O)CH_2-	1-pyrenyl	21
4-biphenylyl	-CH_2-	-CH_2-	4-nitrophenyl	51
4-biphenylyl	-CH_2-	-CH_2-	2-naphthyl	76
4-biphenylyl	-(C=O)-	-(C=O)-	2-naphthyl	60
4-biphenylyl	-CH_2-	-CH_2-	9-phenanthrenyl	52
4-biphenylyl	-(C=O)-	-(C=O)-	9-phenanthrenyl	36

a) All derivatives were identified by ^{1}H-NMR analysis and elementary analysis.

A preliminary investigation of the effect of cation included into the triads having amide linkages on the photo-induced electron transfer rate has been reported[1]. The unsymmetrically bis(substituted) diazacrown

derivative would be a prototype of molecular device switching intramolecular interaction between functional groups through inclusion of various kinds of guest molecules as well as manipulating an intramolecular electron transfer dynamics.

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5. In this work, benzyl chloride and 4-(chloromethyl)biphenyl were also used for chloromethyl derivative.
6. Acid chloride derivatives could be used in the same as chloromethyl derivatives. In this work, benzoyl chloride, phenylacetyl chloride, 4-nitrobenzoyl chloride, 4-nitrophenylacetyl chloride, 2,4-dinitrophenylacetyl chloride and 4-biphenylcarbonyl chloride were also used. Phenylacetyl chloride, 4-nitrophenylacetyl chloride and 2,4-dinitrophenylacetyl chloride were prepared from their acids treated with thionyl chloride Phenylacetic acid was obtained by the hydrolysis of benzyl cyanide in conc. sulfuric acid.
7. 2-(Chloromethyl)naphthalene, 2-naphthoyl chloride, 2-naphthylacetyl chloride, 9-(chloromethyl)anthracene, 9-(chloromethyl)phenanthrene,9-phenanthrenecarbonyl chloride and 1-(chloromethyl)pyrene were also used. 2-Naphtylacetyl chloride was prepared from 2-naphthylacetic acid treated with thionyl chloride. 2-(Chloromethyl)naphthalene was obtained by the chlorination of 2-(hydroxymethyl)naphthalene with phosphorus trichloride in dry benzene. 9-Phenanthrenecarboxaldehyde and 1-pyrenecarboxaldehyde were reduced by sodium boronhydride in dimethylformamide and the resulting alcohol were converted into 9-(chloromethyl)phenanthrene and 1-(chloromethyl)pyrene treated with thionyl chloride in dry benzene.
8. ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): Crown: δ 2.80 (t, -OCH_2CH_2N-NB), δ 2.94 (t, Py-NCH_2CH_2O-), δ 3.62 (t, -OCH_2CH_2N-NB), δ 3.66 (t, Py-NCH_2CH_2O-), δ 3.59 (s,-OCH_2CH_2O-), Nitrobenzene: δ 3.74 (s, N-CH_2-), δ 7.45 (d), δ 8.05 (d), Pyrene: δ 4.35 (s, -CH_2-N), δ 7.98 (t), δ 8.15 (d), δ 8.16 (d), δ 8.02 (s), δ 8.05 (d), δ 8.11 (d), δ 8.10 (d), δ 8.60 (d).
Anal. calcd for $C_{36}H_{41}N_3O_6$: C, 70.68; H, 6.72; N, 6.87; O, 15.69. Found: C, 70.41; H, 6.92; N, 6.57; O, 15.61.
9. 1-Pyrenylacetic acid and 1-pyrenylpropionic acid were also used for n=2 and 3, respectively. 1-Pyrenylacetic acid was synthsized as follows: Methyl methylthiomethyl sulfoxide was reacted with 1-pyrenecarboxyaldehyde and Triton-B in tetrahydrofuran. The condensation product was degraded to ethyl 1-pyrenylacetate by acid-catalysis in dry ethanol. After purification, acid-hydrolysis of the ester gave 1-pyrenylacetic acid. 1-Pyrenylpropionic acid was synthsized as follows: 1-Pyrenecarboxyaldehyde was reacted with triethyl phosphonoacetate and sodium hydride in dimethoxyethane. Hydrogenation of the product on Pd/C in ethanol gave 1-pyrenylpropionic acid.
10. ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): Crown: δ 2.74 (t, -OCH_2CH_2N-NB), δ 2.78 (t, Py-NCH_2CH_2O-), δ 3.56 (t, -OCH_2CH_2N-NB), δ 4.35 (t, Py-NCH_2CH_2O-), δ 3.56 (s,-OCH_2CH_2O-), Nitrobenzene: δ 7.47 (d), δ 8.10 (d), δ 3.70 (s, N-CH_2-), Pyrene: δ 2.58 (t, -$CH_2CH_2CH_2CH_2$-N), δ 1.65 (t, -$CH_2CH_2CH_2CH_2$-N), δ 1.86 (t, -$CH_2CH_2CH_2CH_2$-N), δ 3.34 (t, -$CH_2CH_2CH_2CH_2$-N), δ 7.85 (d), δ 8.09 (d), δ 7.97 (t), δ 8.14 (d), δ 8.15 (d), δ 7.99 (d), δ 8.02 (d), δ 8.08 (d), δ 8.27 (d).
Anal. calcd for $C_{39}H_{47}N_3O_6$: C, 71.64; H, 7.25; N, 6.43; O, 14.68. Found: C, 71.04; H, 7.29; N, 6.37; O, 14.60.

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