S_NAr REACTIONS OF METHYL AND ETHYL 2-NITRO-5-FLUOROBENZOATES IN THE SYNTHESIS OF PYRRO[2,1-c][1,4]BENZODIAZEPINE PRECURSORS

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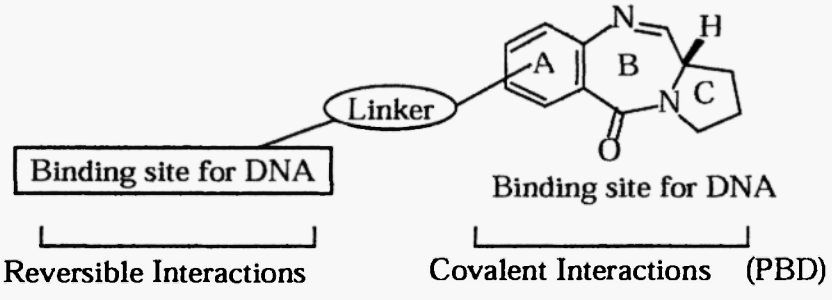
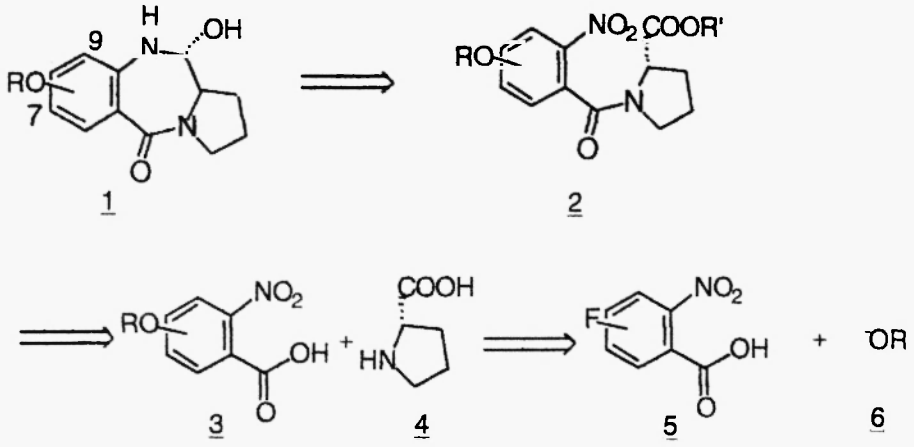
Abstract : The title reaction was investigated as part of an effective synthesis of pyrrolo[2,1-c][1,4]-benzodiazepines possessing a long alkylamino unit at position 7.

There is growing interest in pyrrolo[2,1-c][1,4]benzodiazepine (PBD) ring systems as synthetic targets and as potential anticancer agents. The PBDs are a class of antitumor antibiotics produced by various *actinomycetes* which include anthramycin, tomaymycin, neothramycin and DC-81.[1] These compounds can recognize and bind to preferred sequences of double helical DNA and have potential as therapeutic agents in the treatment of certain genetic disorders including some cancers.[2] They appear to exert their biological activity by reacting covalently in the minor groove of DNA to form an aminal linkage between the electrophilic carbinolamine present at the C-11 position and the N2 of guanine.[3] The preferred bonding sequence involves a 5'-PuGPu motif.[1]



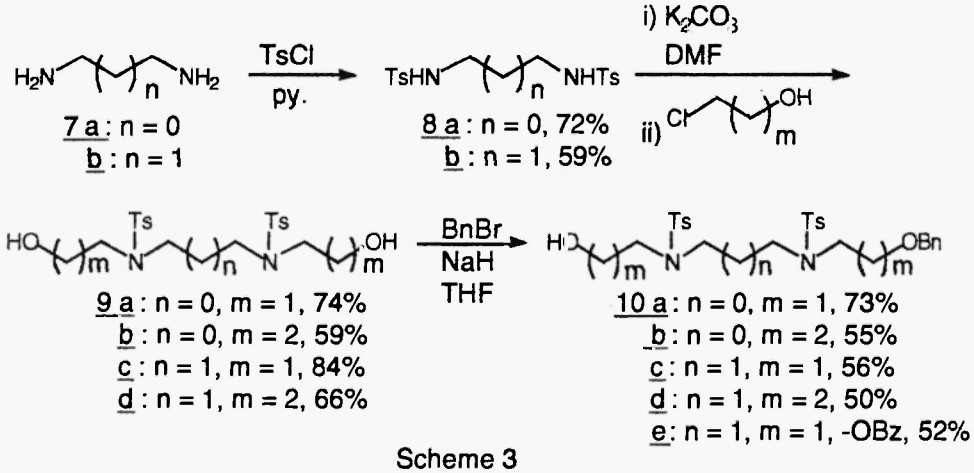
Scheme 1

In the last few years, various strategies have been proposed for the synthesis of these antibiotics and have met with varying degrees of success while exhibiting significant limitations.[4] In order to alter the DNA-recognition ability and selectivity of PBDs (Scheme 1), it was considered desirable to introduce polyaminoalkyl groups as side-chains at the positions 7 and 9 of the A ring of PBD which is known to interact with DNA reversibly. Our strategy for this purpose is shown as Scheme 2. In this connection, we describe below S_NAr (nucleophilic aromatic substitution) reaction of alkyl 2-nitro-5-fluorobenzoates.



Schme 2. Retrosynthetic analysis

The straight-chain polyaminoalkanes **10a-e** were chosen for the ready availability as side-chains interacting with DNA electrostatically. The amino part of 1,2-diaminoethane **7a** or 1,3-diaminopropane (**7b**) was *p*-toluenesulfonylated, metallized, and treated with 2-chloroethanol or 3-chloropropanol, and the diols **9a-d** were thereby obtained. Then the diols **9a-d** were selectively monobenzylated with dilute benzyl bromide in THF in the presence of sodium hydride, producing the corresponding monobenzylalcohols **10a-e** (Scheme 3).

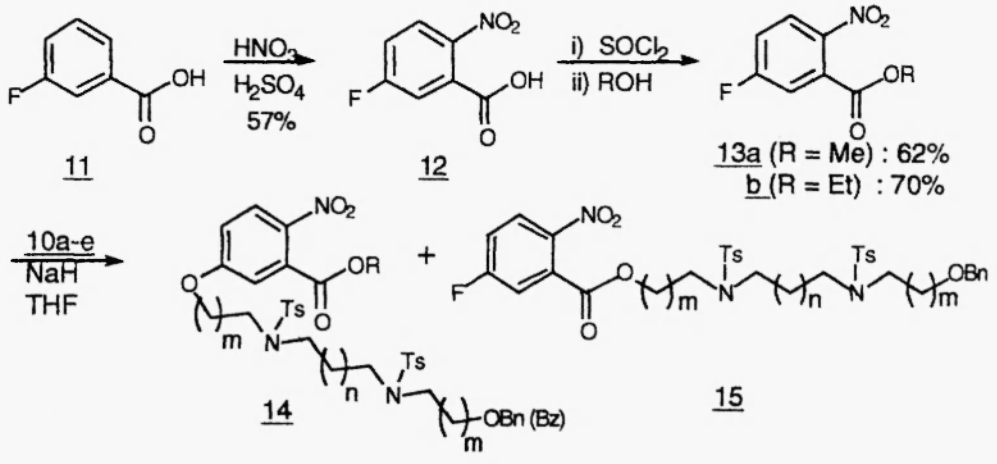


Scheme 3

First, the effectiveness of the S_NAr reaction of the esters **13**, which were obtained by the nitration of 3-fluorobenzoic acid **11**, followed by esterification, was investigated as a method of introduction of the side-chain. For example, the reaction of the ester **13b** with the alcohol **10a** readily took place in THF on treating with sodium hydride, giving the product **14ab** in 59% yield. Thus, the S_NAr reaction is effective as a method of side-chain introduction (Scheme 4). The use of the alcohol **10a** (n=0, m=1), in which the number of methylene groups between the oxygen and the nitrogen atoms is two, gave the S_NAr products **14aa** and **14ab** almost selectively in both cases of the esters **13a** and **13b**, whereas in the case of **10b** (n=0, m=2) in which the methylene-chain is three, the transesterification took place preferentially to give **15bb**. However, in the cases of **10c** (n=1, m=1) and **10d** (n=1, m=2), derivatives of

1,3-propanediamine, the S_NAr products were obtained almost exclusively regardless of the length of methylene-chain between the oxygen and the nitrogen atoms (Table 1). The reason for the difference among these reactions is not clear at present.

Further studies toward the synthesis of conjugated PBD are in progress and will be reported in due course.



Scheme 4

Table 1. S_NAr and transesterification reactions of **13**

alcohol	benzoate	**14** (%)	**15** (%)
10a (n = 0, m = 1)	**13a**	35(**14aa**)	trace
a (n = 0, m = 1)	**13b**	59(**14ab**)	0
b (n = 0, m = 2)	**13b**	6(**14bb**)	39(**15bb**)
c (n = 1, m = 1)	**13b**	72(**14cb**)	trace
d (n = 1, m = 2)	**13b**	65(**14db**)	---
e (n = 1, m = 2)	**13a**	45(**14ea**)	---

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EXPERIMENTAL

Experimemtal details are same as described before.[5]

1,2-Bis(tosylamino)ethane 8a To a solution of 1,2-diaminoethane (6.0 g, 0.10 mol) in pyridine (130 ml) was added p-toluenesulfonyl chloride (384 g, 0.20 mol) in small portions over a period of 30 min at 0 °C. The mixture was stirred at 60 °C for 6 h. Then water was added and the precipitate was collected, recrystallized from acetone to afford **8a** (27.6 g, 72 %) as colorless needles. mp 164-165 °C (acetone); ^{1}H NMR (270 MHz, $CDCl_3$) δ: 2.43 (6H, s), 3.04-3.08 (4H, m), 5.05 (2H, br. s), 7.25-7.74 (8H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) d: 21.5 (q), 43.0 (t), 127.1 (d), 129.8 (d), 136.4 (s), 143.8 (s); IR υmax (film): 3286, 1156, 663, 550 cm^{-1}; Anal. Calcd for $C_{16}H_{20}O_4N_2S_2$: C, 52.16; H, 5.48; N, 7.61. Found: C, 52.33; H, 5.52; N, 7.59.

1,3-Bis(tosylamino)propane 8b was prepared in a similar manner in 59 % yield as colorless needles; mp 141.0-142.0 °C (ethyl acetate-hexane); ^{1}H NMR (270 MHz, CDCl3) δ: 1.58-1.72 (2H, m), 2.41 (6H, s), 2.99 (4H, q, J = 6.5 Hz), 5.12 (2H, t, J = 6.5 Hz), 7.29 (4H, d, J = 8.1 Hz), 7.72 (4H, d, J = 8.1 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 29.7, 39.8, 127.0, 129.8, 136.7, 143.5; IR υmax (nujol): 3248, 1156 cm^{-1}; *Anal.* Calcd for $C_{17}H_{22}O_4N_2S_2$: C, 53.39; H, 5.80; N, 7.32. Found: C, 53.43; H, 5.80; N, 7.16.

N, N'-Bistosyl-1,2-bis(2-hydroxyethylamino)ethane 9a. A General Procedure

To a solution of **8a** (13.2 g, 34 mmol) in DMF (80 ml) was added potassium carbonate (23.4 g, 170 mmol), and the mixture was refluxed for 30 min. Then to the mixture was added a solution of 2-chloroethanol (41.1 g, 510 ml) in DMF (20 ml) at the same temperature, and the mixture was refluxed over night. Then water was added to the mixture, and the filtrate was collected, recrystallized from ethanol to afford **9a** (11.6 g, 74.4%) as colorless needles: mp 155-156 °C (ethanol); ^{1}H NMR (270 MHz, $CDCl_3$) δ: 2.44 (6H, s), 2.86 (2H, br.s), 3.25 (4H, t, J = 5.0 Hz), 3.41 (4H, s), 3.81 (4H, t, J = 5.0 Hz), 7.31-7.74 (8H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 50.4, 53.1, 61.1, 127.4, 129.9, 135.0, 143.8; IR υmax (film): 3289, 1332, 1155, 717, 549, 516 cm^{-1}; *Anal.* Calcd for $C_{20}H_{28}O_6N_2S_2$: C, 52.62; H, 6.19; N, 6.14. Found: C, 52.35; H, 6.25; N, 6.09.

N, N'-Bistosyl-1,2-bis(3-hydroxypropylamino)ethane 9b was prepared in a similar manner in 59 % yield as colorless needles; mp 138-139 °C (ethanol); ^{1}H NMR (270 MHz, CDCl3) δ: 1.74-1.86 (4H, m), 2.17 (2H, br.s), 2.44 (6H, s), 3.25 (4H, t, J = 6.8 Hz), 3.31 (4H, s), 3.68-3.80 (4H, m), 7.30-7.72 (8H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 31.4, 46.9, 49.4, 58.9, 127.2, 129.9, 135.4, 143.8; IR υmax (film): 3354, 1341, 1154, 1086, 811, 648, 566, 548 cm^{-1}; *Anal.* Calcd for $C_{22}H_{32}O_6N_2S_2$: C, 54.52; H, 6.66; N, 5.78. Found: C, 54.33; H, 6.80; N, 5.52.

N, N'-Bistosyl-1,3-bis(2-hydroxyethylamino)propane 9c was prepared in a similar manner in 84 % yield as a colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.99 (2H, quin, J = 7.3 Hz), 2.43 (6H, s), 2.83 (2H, t, J = 5.4 Hz), 3.14-3.28 (8H, m), 3.77 (4H, q, J = 5.4 Hz), 7.30-7.72 (8H, m); ^{13}C NMR (67.8 MHz, CDCl3) δ: 21.5, 28.9, 48.2, 52.0, 61.6, 127.2, 129.8, 135.4, 143.6; IR υmax (neat): 3450, 1322, 1149 cm^{-1}.

N, N'-Bistosyl-1,3-bis(3-hydroxypropylamino)propane 9d was prepared in a similar manner in 66 % yield as a colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.70-1.96 (6H, m), 2.43 (6H, s), 2.52 (2H, br. s, D_2O exchangeable), 3.15 (4H, t, J = 7.4 Hz), 3.21 (4H, t, J = 6.8 Hz), 3.72 (4H, q, J = 5.5 Hz), 7.27-7.70 (8H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 28.9, 31.7, 46.1, 47.5, 59.0, 127.1, 129.8, 135.7, 143.6; IR υmax (neat): 3370, 1327, 1148 cm^{-1}.

N, N'-Bistosyl-1(2-benzyloxyethylamino)-2(2-hydroxyethylamino)ethane 10a. A General Procedure

To a solution of the diol **9a** (912 mg, 2.0 mmol) in THF (20 ml) was added 50 % sodium hydride (96 mg, 2.0 mmol), and the suspension was refluxed for 30 min. To the mixture was added a solution of benzyl bromide (0.29 ml, 2.4 mmol) in THF (10 ml) at the same temperature, and the mixture refluxed over night.Then water (10 ml) was added to the mixture, and the organic layer was extracted with ethyl acetate (10 ml, 3 times). The combined organic layer was washed with brine (10 ml), and dried over magnesium sulfate. The solvent was removed in vacuo, and the residue was further purified by column chromatography on silica gel (30 g) with ethyl acetate and hexane (1:1, v/v) to afford monobenzyl alcohol **10a** (792 mg, 72.5 % yield) as colorless needles; mp 106-107 °C (Ethyl acetate-Hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ: 2.19 (1H, br s, -OH), 2.43 (6H, s), 3.13 (2H, t, J = 5.1 Hz), 3.32-3.40 (2H, m), 3.38 (4H, s), 3.63 (4H, t, J = 5.1 Hz), 4.48 (2H, s), 7.24-7.72 (13H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 49.6, 49.7, 49.9, 52.7, 61.2, 69.4, 73.2, 127.2, 127.3, 127.8, 127.9, 128.4, 129.8, 129.8, 135.4, 135.7, 143.5, 143.6; IR υmax (film): 3528, 1340, 1158, 1089, 718, 549 cm^{-1}; *Anal.* Calcd for $C_{27}H_{34}O_6N_2S_2$: C, 59.32; H, 6.27; N, 5.12. Found: C, 59.10; H, 6.33; N, 5.07.

N, N'-Bistosyl-1(3-benzyloxypropylamino)-2(3-hydroxypropylamino)ethane 10b was prepared in a similar manner in 55 % yield as colorless needles; mp 111-112 °C (Ethyl acetate-Hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.72-1.93 (4H, m), 2.28 (1H, br.s), 2.42 (6H, s), 3.18-3.29 (6H, m), 3.50 (2H, t, J = 6.0 Hz), 3.66-3.74 (2H, m), 4.47 (2H, s), 7.25-7.72 (8H, m); ^{13}C NMR (67.8 MHz, CDCl3) δ: 21.5, 29.0, 31.3, 46.8, 47.4, 48.8, 49.1, 58.8, 67.1, 72.9, 127.1, 127.2, 127.6, 127.7, 128.4, 129.8, 129.9, 135.4, 135.6, 138.2, 143.6, 143.7; IR υmax (film): 3543, 1341, 1158, 1090, 726, 549 cm^{-1}; *Anal.* Calcd for $C_{29}H_{38}O_6N_2S_2$: C, 60.60; H, 6.66; N, 4.87. Found: C, 60.32; H, 6.67; N, 4.86.

N, N'-Bistosyl-1(2-benzyloxyethylamino)-3(2-hydroxyethylamino)propane 10e was prepared in a similar manner in 56 % yield as a colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.93 (2H, quint, J = 7.0 Hz), 2.41 (3H, s), 2.42 (3H, s), 2.51 (1H, t, J = 5.9 Hz, D2O exchangeable), 3.07-3.16 (4H, m), 3.21-3.30 (2H, m), 3.34 (2H, t, J = 5.4 Hz), 3.62 (2H, t, J = 5.4 Hz), 3.67 (2H, q, J = 5.4 Hz), 4.45 (2H, s), 7.22-7.70 (13H, m); 13C NMR (67.8 MHz, CDCl3) δ: 21.5, 28.4, 47.4, 48.2, 48.5, 51.9, 61.5, 69.5, 73.2, 127.1, 127.2, 127.7, 127.8, 128.4, 129.7, 129.8, 135.5, 136.2, 137.7, 143.3, 143.5; IR υmax (neat): 3485, 1330, 1152 cm^{-1}; *Anal.* Calcd for $C_{28}H_{36}O_6N_2S_2$: C, 59.98; H, 6.47; N, 5.00. Found: C, 59.83; H, 6.51; N, 4.85.

N, N'-Bistosyl-1(3-benzyloxypropylamino)-3(3-hydroxypropylamino)propane 10d was prepared in a similar manner in 50 % yield as a colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ : 1.71-1.92 (6H, m), 2.39 (1H, t, J = 5.8 Hz, D_2O exchangeable), 2.42 (6H, s), 3.07-3.25 (8H, m), 3.47 (2H, t, J = 5.9 Hz), 3.68 (2H, q, J = 5.8 Hz), 4.46 (2H, s), 7.25-7.69 (13H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.5, 28.6, 29.3, 31.6, 45.8, 46.4, 46.8, 47.4, 58.7, 67.3, 73.0, 127.1, 127.7, 128.4, 129.7, 129.8, 135.7, 136.2, 138.1, 143.3, 143.5; IR υmax (neat): 3500, 1328, 1150 cm^{-1}; *Anal.* Calcd for $C_{30}H_{40}O_6N_2S_2$: C, 61.20; H, 6.85; N, 4.76. Found: C, 61.11; H, 6.82; N, 4.62.

N, N'-Bistosyl-1(2-benzoyloxyethylamino)-2(2-hydroxyethylamino)ethane 10e was prepared in a similar manner in 52 % yield as colorless needles; mp 109-110 °C (ethanol); ^{1}H NMR (270 MHz, $CDCl_3$) δ: 2.37 (3H, s), 2.39 (3H, s), 2.62 (1H, br.s), 3.24 (2H, t, J = 5.4 Hz), 3.30-3.58 (6H, m), 3.76 (2H, t, J = 5.4 Hz), 4.42-4.50 (2H, m), 7.20-8.00 (13H, m); ^{13}C NMR (67.8 MHz, CDCl3) δ: 21.4 (q), 48.3 (t), 49.1 (t), 49.7 (t), 52.6 (t), 61.4 (t), 62.4 (t), 127.0 (d), 127.1 (d), 128.3 (d), 129.5 (s), 129.6 (d), 129.7 (d), 129.8 (d), 133.1 (d), 135.2 (s), 135.5 (s), 143.6 (s), 143.7 (s), 166.2 (s); IR υmax (neat): 3500, 1712, 1339, 1268, 1152 cm^{-1}; *Anal.* Calcd for $C_{27}H_{32}O_7N_2S_2$: C, 57.84; H, 5.76; N, 5.00. Found: C, 57.55; H, 5.57; N, 4.94.

2-Nitro-5-fluorobenzoic acid 12. To a solution of conc. nitric acid (30 ml) and conc. sulfuric acid (30 ml) was added m-fluorobenzoic acid **11** (14 g, 0.1 mol) in a small portions over 1 h at 10-20 °C, and the mixture was stirred for more 2 h at room temperature Then the mixture was poured into ice, and the precipitate was collected. The product was recrystallized from ethyl acetate/hexane to afford the nitro benzoic acid **12** (10.5 g, 56.8 %) as colorless plates.^{1}H NMR (270 MHz, $CDCl_3$) δ: 7.36 (1H, m), 7.53 (1H, dd, J = 4.6, 7.9 Hz), 8.00 (1H, dd, J = 2.6, 7.9 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 117.6 (J_{C-F} = 26.9 Hz), 119.3 (J_{C-F} = 23.2 Hz), 126.9 (J_{C-F} = 8.6 Hz), 129.2 (J_{C-F} = 8.5 Hz), 144.3, 164.2 (J_{C-F} = 258.8 Hz), 168.6; υ_{max} (film): 1715, 1590, 1528, 1351, 1223 cm-1; MS (m/z) : 185 (M^+), 155, 141, 111, 83 (100%); HRMS 185.0125 (M^+, 185.0124 calcd for $C_7H_4O_4NF$).

Methyl 2-nitro-5-fluorobenzoate 13a. To a solution of 2-nitro-5-fluorobenzoic acid **12** (2.78 g, 15 mmol) in benzene (30 ml) was added thionyl chloride (2.2 cm^3, 30 mmol), and the mixture was refluxed for 1 h. To the mixture was added methanol (10 cm^3) at room temperature and the mixture was stirred for 20 min at the same temparature. After addition of water (10 ml), the organic layer was extracted with ethyl acetate (15 ml, 3 times). The combined organic layer was washed with brine (10 ml), dried over magnesium sulfate, and the solvent was removed in vacuo. This residue was further purified by column chromatography on silica gel (30 g) with ethyl acetate and hexane (1:4, v/v) to afford the methyl ester **13a** (3.47 g, 62.7 % yield) as a colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ: 3.95 (3H, s), 7.27-7.35 (1H, m), 7.36-7.42 (1H, m), 8.02 (1H, dd, J = 8.9, 4.6 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 53.5, 116.9 (J_{C-F} = 25.6 Hz), 118.3 (J_{C-F} = 23.2 Hz), 126.8 (J_{C-F} = 9.7 Hz), 130.7 (J_{C-F} = 8.8 Hz), 143.8, 164.4 (J_{C-F} = 257.13 Hz), 164.7; υ_{max} (film): 1740, 1591, 1534, 1438, 1349 cm-1; MS (m/z) : 199 (M^+), 168 (100%), 152, 94; HRMS 199.0281 (M^+, 199.0281 calcd for $C_8H_6O_4NF$).

Ethyl 2-nitro-5-fluorobenzoate 13b was prepared in a similar manner in 70 % yield as a colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.37 (3H, t, J = 7.3 Hz), 4.41 (2H, q, J = 7.3 Hz), 7.26-7.42 (2H, m), 7.97-8.05 (1H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 13.7, 62.9, 116.9 (J_{C-F} = 25.6 Hz), 118.2 (J_{C-F} = 24.3 Hz), 126.8 (J_{C-F} = 9.7 Hz), 131.1 (J_{C-F} = 8.7 Hz), 143.8, 164.3, 164.4 (J_{C-F} = 258.3 Hz); υ_{max} (film): 1737, 1591, 1537, 1350, 1289, 1215, 1089 cm^{-1}; MS (m/z) : 213 (M^+), 185, 168 (100%), 153, 111, 94; HRMS 213.0432 (M+, 213.0437 calcd for C9H8O4NF).

General Procedure for the S_NAr Reaction of 13 with 10. A typical example for **14aa**. To a solution of the benzyl ether **10a** (745 mg, 1.36 mmol) in THF (20 ml) was added sodium hydride (131 mg, 4.09

mmol), and the mixture was refluxed for 40 min. Then to the suspension was added a solution of the ester **13a** (815 mg, 4.09 mmol) in THF (10 ml), and refluxed over night. After addition of water (10 ml), the organic layer was extracted with ethyl acetate (15 ml, 3 times). The combined organic layer was washed with brine (10 ml), dried over sodium sulfate, and the solvent was removed in vacuo. This residue was further purified by column chromatography on silica gel (30 g) with ethyl acetate and hexane (1:2, v/v) to afford the methyl ester **14aa** (348 mg, 35.3 %) as a colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ: 2.41 (6H, s), 3.32-3.40 (4H, m), 3.43-3.50 (4H, m), 3.60-3.73 (2H, m), 3.93 (3H, s), 4.14 (2H, t, J = 5.7 Hz), 4.47 (2H, s), 6.90-8.03 (16H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.4, 48.9, 49.6, 49.8, 50.1, 53.4, 67.6, 69.4, 73.2, 114.8, 116.1, 126.6, 126.7, 127.1, 127.2, 127.8, 1284, 129.8, 129.9, 131.1, 135.7, 135.8, 137.7, 140.4, 143.7, 143.8, 162.0, 165.8; υ_{max} (film): 1739, 1590, 1534, 1344, 1304, 1157 cm^{-1}; MS (m/z) : 570 (M^+-TsO), 469, 318, 226, 155, 91 (100%); HRMS 570.1927 (M^+-TsO, 570.1910 calcd for $C_{28}H_{32}O_8N_3S$).

15bb was prepared in a similar manner in 39 % yield as a colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.78-2.10 (4H, m), 2.42 (6H, m), 3.16-3.35 (8H, m), 3.49 (2H, t, J = 6.1 Hz), 4.39 (2H, t, J = 6.1 Hz), 4.47 (2H, s), 7.20-8.04 (16H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 21.4, 27.7, 29.0, 47.1, 47.4, 48.7, 49.0, 63.8, 67.1, 72.8, 117.1 ($J_{C\text{-}F}$ = 25.6 Hz), 118.2 ($J_{C\,F}$ = 23.2 Hz), 126.7($J_{C\,F}$ = 10.4 Hz), 127.2, 127.2, 127.5, 127.6, 128.3, 129.7, 129.8, 129.7-129.8 (br), 130.8, 135.3, 135.7, 138.3, 143.5, 143.6, 164.2 ($J_{C\text{-}F}$ = 258.3 Hz), 164.2; υ_{max} (neat): 1725, 1578, 1328, 1290, 1149 cm^{-1}.

14cb was prepared in a similar manner in 72 % yield as a colorless oil: ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.35 (3H, t, J = 7.2 Hz), 1.88-2.02 (2H, m), 2.34 (6H, s), 3.16-3.28 (4H, m), 3.32 (2H, t, J = 5.7 Hz), 3.42 (2H, t, J = 5.9 Hz), 3.59 (2H, t, J = 5.7 Hz), 4.16 (2H, t, J = 5.9 Hz), 4.39 (2H, q, J = 7.2 Hz), 4.41 (2H, s), 6.90-7.99 (16H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 13.7 (q), 21.4 (q), 28.3 (t), 47.2 (t), 47.3 (t), 47.7 (t), 48.6 (t), 62.4 (t), 62.4 (t), 67.6 (t), 69.2 (t), 73.0 (t), 114.6 (d), 115.8 (d), 126.5 (d), 127.0(d), 127.0 (d), 127.5 (d), 127.6 (d), 128.3 (d), 129.6 (d), 129.7 (d), 131.3 (d), 135.8 (s), 136.0 (s), 137.7 (s), 140.0 (s), 143.3 (s), 143.6 (s), 161.8 (s), 165.7 (s); υ_{max} (neat): 1726, 1580, 1332, 1292, 1150 cm^{-1}.

14db was prepared in a similar manner in 65 % yield as a colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ: 1.36 (3H, t, J = 7.3 Hz), 1.76-2.14 (6H, m), 2.38 (3H, s), 2.41 (3H, s), 3.08-3.22 (6H, m), 3.28 (2H, t, J = 6.9 Hz), 3.46 (2H, t, J = 5.9 Hz), 4.04 (2H, t, J = 5.9 Hz), 4.39 (2H, q, J = 7.3 Hz), 4.45 (2H, s), 6.90-8.05 (16H, m); 13C NMR (67.8 MHz, CDCl3) δ: 13.7, 21.4, 28.4, 28.5, 29.1, 45.6, 46.3, 46.6, 46.7, 62.4, 66.0, 67.2, 72.8, 114.6, 115.8, 126.5, 127.0, 127.5, 128.3, 129.7, 129.7, 131.4, 135.8, 136.0, 138.2, 139.9, 143.3, 143.5, 162.4, 165.5; υ_{max} (neat): 1724, 1578, 1328, 1290, 1149 cm^{-1}.

14ea was prepared in a similar manner in 45 % yield as a colorless oil; 1H NMR (270 MHz, $CDCl_3$) δ: 1.26 (3H, t, J = 7.3 Hz), 2.29 (6H, s), 2.31 (3H, s), 3.39 (4H, s), 3.42-3.52 (4H, m), 4.14 (2H, t, J = 5.4 Hz), 4.30 (2H, q, J = 5.4 Hz), 4.39 (2H, t, J = 5.4 Hz), 6.82-8.00 (16H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 13.7, 21.4 , 48.5, 49.1, 49.2, 49.9, 62.5, 62.6, 67.7, 114.7, 116.0, 126.6, 127.0, 127.1, 128.4, 129.5, 129.6, 129.8, 129.9, 131.4, 133.2, 135.3, 135.5, 140.3, 143.9, 144.0, 161.8, 165.7, 166.1.

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