Syntheses of Mannosidic Disaccharides from Derivatives of Ethylthio α-D-Mannopyranoside

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Derivatives of ethylthio α-D-mannopyranoside as glycosyl donors are compared in coupling efficiency and stereoselectivity with varying thiophilic promoters from methyl triflate (MeOTf), dimethyl(methylthio)sulfonium triflate (DMTST) to iodonium dicollidine perchlorate (IDCP), solvents and glycosyl acceptors. IDCP was the most efficient promoter in coupling of perbenzylated ethylthio-α-D-mannopyranosides (**1** and **2**), giving α-D-mannosyl disaccharides preferentially, whereas inactive in coupling of 4,6-*O*-benzylidene derivatives **3** and **4**. MeOTf and DMTST promoted coupling of 4,6-*O*-benzylidene derivatives **3** and **4**, but β-D-mannopyranosyl disaccharides were formed preferentially. Coupling reaction was retarded as solvent polarity decreased.

Introduction

Mannosidic linkages are present in common core oligosaccharides of *N*-linked glycoproteins[1] and some bacterial *O*-antigens.[2] Their biological importance has led to develop synthetic methods for tailored mannosidic oligosaccharides. So far a few achievements have been made in stereoselective syntheses by applying anomeric stability[3] or intramolecular aglycon delivery.[4-5] Thus it is desirable to develop more efficient and more stereocontrolled methods in coupling of mannosyl residues.

Thio glycosides, fairly stable through chemical transformations such as OH protection-deprotection steps, but specifically cleaved by thiophiles, have served as versatile glycosyl donors in armed-disarmed chemospecific glycosidation.[6,7-9] Selectivity of IDCP for perbenzylated thioglucosides resulted in exclusive formation of α-glucosidic disaccharides (1,2-*cis*-stereochemical relationship) with partially-benzoylated thioglucosides. The produced thio-glycosyl disaccharide donor having benzoyl groups was extended to trisaccharides by NIS-TfOH promoter.[9-11]

In this paper derivatives of ethylthio α-D-mannopyranoside have been examined as a glycosyl donor varying glycosyl accepters, solvents and promoters. IDCP,[7,12] MeOTf,[13] and DMTST[10,14,15] promoters were compared in terms of efficiency and stereochemical outcomes.[16]

Experimental

General. Concentration was performed under reduced pressure at below 40 °C (bath). CH_2Cl_2 and ether were dried over P_2O_5 and Na-benzophenone, respectively. Freshly distilled solvents were used for reactions. NMR spectra were recorded in chloroform-*d* solutions referenced to internal TMS (a Varian VXR-200 or a JEOL JNM-LA400 spectrometer). Assignments were based on DEPT, 2D COSY, and proton-carbon correlation experiments. Flash column chromatography was performed on silica gel Merck 60 (Art 7734 70-230 mesh and Art 9385 230-400 mesh) with toluene-EtOAc, 15 : 1. TLC was conducted on plates coated with a 0.2 mm layer of silica gel $60F_{254}$ (Merck) with toluene-EtOAc, 5 : 1; the components were located by charring the plate with 5% sulfuric acid.

Glycosylation reactions were performed in the following procedures according to Table 1, unless otherwise stated.

To solution of a donor (0.35 mmol) and an acceptor (0.27 mmol) in dichloromethane-ether (2 : 5, 10 mL) or dichloromethane (10 mL) was added freshly powdered MS 5 Å, and the mixture was stirred for 30 min at room temperature (5-10 °C for DMTST). To the mixture was added, with stirring, the promoter (0.81 mmol), and stirring was continued for the reaction time at given temperature (Table 1). The reaction mixtures were purified as followed depending on promoter.

Iodonium dicollidine perchlorate (IDCP)[17]. The precipitate was filtered off through Celite pad, and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with 1 M $Na_2S_2O_3$ and water, dried (Na_2SO_4), concentrated, and purified on silica gel column.

Methyl trifluoromethanesulfonate (MeOTf) and Dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST)[11]. Triethylamine (2.66 mmol) was added to the mixture after given reaction time and stirring was continued for 10 min. The mixture was filtered through Celite pad, concentrated, and purified on silica gel column.

Methyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (D1α) and methyl *O*-(2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (D1β). **D1α** and **D1β** were obtained from **1** (204.5 mg) and **5** (125 mg) in 4 different conditions reported in Table 1. The produced mixture was flash chromatographed on silica gel eluting with toluene-EtOAc (15 : 1, v/v) : R_f 0.75 for **1**, 0.12 for **5**, 0.50 for **D1α**, and 0.44 for **D1β** (toluene-EtOAc, 5 : 1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D1α** δ 7.36-7.14 (m, 35H, aromatic H), 5.01-4.42 (m, 16H, H-1, H-1', and $C_6H_5CH_2$), 4.03-3.38 (m, 12H), 3.30 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D1α** δ 138.6-127.3 (aromatic C), 98.1 (C-1'), 97.7 (C-1), 82.0, 79.9, 79.4, 77.5, 75.6, 74.9, 74.78, 74.75, 74.6, 73.13, 73.1, 72.3, 71.9, 69.7, 69.0, 65.7, 54.9 ($O\underline{C}H_3$), $[\alpha]_D^{24}$+23.9 (*c* 1.81, $CHCl_3$), ES(+)MS 1004.0 [100, $(M+NH_4)^+$]; ^{1}H NMR ($CDCl_3$, 400 MHz) for **D1β** δ 7.43-7.18 (m, 35H, aromatic H), 5.03-4.46 (m, 16H, H-1, H-1', and C_6H_5

Table 1. Coupling of Thiomannosyl donors with acceptors

Entry	Donor	Acceptor	Promotor	Solvent	Temperature	Time	Disacchride : % yield (α/β)
1	**1**	**5**	IDCP	C-E(2/5)	r.t.	10 min	D1α; Man α 6Glc, D1β; Man β 6Glc, 78 (1.5/1)
2	**1**	**5**	IDCP	C	r.t.	43 min	D1α; Man α 6Glc, D1β; Man β 6Glc, 53 (1/1)
3	**1**	**5**	MeOTf	C-E(2/5)	r.t.	41 hr	D1α; Man α 6Glc, D1β; Man β 6Glc, 84 (1.5/1)
4	**1**	**5**	MeOTf	C	r.t.	48 hr	D1α; Man α 6Glc, D1β; Man β 6Glc, 72 (1.35/1)
5	**1**	**6**	IDCP	C-E(2/5)	r.t.	5 min	D2α; Man α 3Glc, D2β; Man3 β Glc, 97 (4.7/1)
6	**1**	**7**	IDCP	C-E(2/5)	r.t.	8 min	D3α; Man α 6Glc, D3β; Man β 6Glc, 79 (3/1)
7	**1**	**8**	IDCP	C-E(2/5)	r.t.	2 min	D4α; Man α 3GlcNPhth, 96 (1/0)
8	**1**	**8**	DMTST	C	5~10 °C	30 min	D4α; Man α 3GlcNPhth, 36 (1/0)
9	**2**	**6**	IDCP	C-E(2/5)	r.t.	10 min	D5α; Man α 3Glc, D5β; Man β 3Glc, 89 (2.2/1)
10	**2**	**6**	MeOTf	C	r.t.	48 hr	D5α; Man α 3Glc, D5β; Man β 3Glc, 49 (3.6/1)
11	**2**	**7**	MeOTf	C	r.t.	24 hr	Decomposed and a Trace of 12*
12	**2**	**10**	IDCP	C-E(2/5)	r.t.	35 min	D6α-3; Man α 3Gal : 36(1/0), D6α-2; Man α 2Gal : 29(1/0)
13	**3**	**5**	IDCP	C	r.t.	6 hr	D7β; Man β 6Gal, 12(0/1)
14	**3**	**6**	IDCP	C	r.t.	22 hr	D8β; Man β 3Gal, 10(0/1)
15	**3**	**7**	MeOTf	C	r.t.	24 hr	D9α; Man α 6Glc, D9β; Man β 6Glc, 58 (1/2.4)
16	**4**	**5**	DMTST	C	5~10 °C	4.5 hr	D10α; Man α 6Glc, D10β; Man β 6Glc, 55 (1/7.1)
17	**4**	**6**	IDCP	C-E(2/5)	r.t.	20 hr	No reaction
18	**4**	**7**	DMTST	C	5~10 °C	4 hr	12*, 15
19	**4**	**7**	MeOTf	C	r.t.	25 hr	12*, 41
20	**4**	**8**	IDCP	C-E(2/5)	r.t.	20 hr	No reaction
21	**4**	**9**	IDCP	C-E(2/5)	r.t.	44 hr	No reaction
22	**4**	**9**	DMTST	C	5~10 °C	6 hr	D11α; Man α 2Glc, D11β; Man β 2Glc, 55 (1/2.5)
23	**4**	**10**	DMTST	C	5~10 °C	7 hr	D13β-3; Man β 3Glc : 30 (0/1), D13β-2; Man β 2Glc : 32 (0/1)
24	**4**	**10**	MeOTf	C	r.t.	25 hr	D13β-3; Man β 3Glc : 24 (0/1), D13β-2; Man β 2Glc : 23 (0/1)
25	**11**	**6**	IDCP	C-E(2/5)	r.t.	24 hr	No reaciton

1) No reaction means starting compounds were recovered. 2) * MPM migration occurred. 3) Solvents C for CH_2Cl_2 E for Et_2O.

$C\underline{H}_2$), 4.18-3.37 (m, 12H), 3.30 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D1β** δ 138.8-127.3 (aromatic C), 101.4 (C-1'), 97.7 (C-1), 82.2, 82.1, 79.8, 77.6, 75.9, 75.6, 75.1, 74.9, 74.6, 73.6, 73.5, 73.4, 73.2, 71.5, 69.72, 69.7, 68.2, 55.0 (OCH_3), $[\alpha]_D^{24}$+6.84 (*c* 2.42, $CHCl_3$).

Methyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D2α) and methyl O-(2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D2β). Glycosidation of **1** (141.3 mg) with **6** (60 mg) using IDCP yielded a mixture. Flash chromatography gave **D2α** (115 mg, 80%) and **D2β** (24.3 mg, 17%) : R_f 0.63 for **1**, 0.22 for **6**, 0.53 for **D2α**, and 0.40 for **D2β** (toluene-EtOAc, 5 : 1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) for **D2α** δ 7.48-7.05 (m, 30H, aromatic H), 5.49 (d, 1H, $J_{1',2'}$=1.44 Hz, H-1'), 5.48 (s, 1H, $C_6H_5C\underline{H}$), 4.91-4.34 (m, 10 H, $C_6H_5C\underline{H}_2$), 4.62 (s, 1H, H-1), 4.30 (t, 1H, H-3), 4.23 (dd, 1H, $J_{5,6a}$=4.88 Hz, $J_{6a,6b}$=10.26 Hz, H-6a), 4.14-4.10 (m, 2H, H-4' and H-5'), 3.89-3.86 (m, 1H, H-3'), 3.84-3.80 (m, 1H, H-5), 3.79-3.78 (m, 1H, H-2'), 3.70-3.60 (m, 3H, H-6b, H-6a', and H-6b'), 3.51 (t, 1H, $J_{3,4}$= 9.52 Hz, $J_{4,5}$=9.52 Hz, H-4), 3.40 (dd, 1H, $J_{1,2}$=3.68 Hz, $J_{2,3}$= 9.52 Hz, H-2), 3.37 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D2α** δ 139.0-125.2 (aromatic C), 101.8 ($C_6H_5\underline{C}H$), 98.7 (C-1), 97.6 (C-1'), 82.7 (C-4), 79.6 (C-3'), 77.9 (C-2), 74.8 ($C_6H_5\underline{C}H_2$), 74.6, 74.0 (C-2'), 73.4 (C-3 and $C_6H_5\underline{C}H_2$), 73.1 ($C_6H_5\underline{C}H_2$), 71.6 ($C_6H_5\underline{C}H_2$), 71.4 ($C_6H_5\underline{C}H_2$), 69.0 (C-6), 68.8 (C-6'), 61.8 (C-5), 55.3 (OCH_3); ^1H NMR ($CDCl_3$, 400 MHz) for **D2β** δ 7.48-7.15 (m, 30H, aromatic H), 5.51 (s, 1 H, $C_6H_5C\underline{H}$), 4.92-4.40 (m, 12H, $C_6H_5C\underline{H}_2$, H-1, and H-1'), 4.22 (dd, 1H), 4.19 (t, 1H), 3.94 (t, 1H), 3.85-3.77 (m, 2H), 3.72-3.61 (m, 4H), 3.52 (dd, 1H), 3.40-3.37 (m, 4H), 3.32-3.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D2β** 139.2-126.2 (aromatic C), 101.9 ($C_6H_5\underline{C}H$), 101.4 (C-1'), 98.5 (C-1), 82.6 (C-4), 80.1, 76.0, 75.1, 74.7, 73.8, 73.6, 73.3, 71.6, 69.4 and 68.9 (C-6 and C-6'), 62.5 (C-5), 55.3 (OCH_3), $[\alpha]_D^{24}$+ 6.26 (*c* 0.45, $CHCl_3$).

2,3,4,6-Tetra-*O*-benzyl-α-*D*-mannopyranosyl-(1→6)-1,2 : 3,4-di-*O*-isopropylidene-α-D-galactopyranose (D3α) and 2,3,4,6-Tetra-*O*-benzyl-β-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (D3β). Glycosidation of **1** (176.3 mg) with **7** (65.4 mg) using IDCP yielded a mixture. Flash chromatography gave **D3α** (115.8 mg, 59%) and **D3β** (38.5 mg, 20%) : R_f 0.7 for **1**, 0.06 for **7**, 0.49 for **D3α** and 0.38 for **D3β** (toluene-EtOAc, 5 : 1); ^1H NMR ($CDCl_3$, 400 MHz) for **D3α** δ 7.39-7.17 (m, 20H, aromatic H), 5.52 (d, 1H, $J_{1,2}$=5.4 Hz, H-1), 5.02 (s, 1H, H-1'), 4.87 (d, 1H, *J*=10.72 Hz), 4.74-4.49 (m, 8H, $C_6H_5C\underline{H}_2$), 4.32 (s, 1H), 4.15 (d, 1H, *J*=7.6 Hz), 4.04-3.68 (m, 9H), 1.50-1,23 (12H, $C(C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D3α** δ 138.6-127.4 (aromatic C), 109.3 ($\underline{C}_a(CH_3)_2$), 108.5 ($\underline{C}_b(CH_3)_2$), 97.2 (C-1'), 96.3 (C-1), 80.0, 75.1, 74.8, 74.5, 73.3, 72.3, 72.0, 70.9, 70.62, 70.55, 69.1, 65.3, 65.2, 26.1, 26.0, 24.9, and 24.5 ($C(\underline{C}H_3)_2$), $[\alpha]_D^{22}$-4.20 (*c* 1.65, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) for **D3β** δ 7.34-7.15 (m, 20 H, aromatic H), 5.60 (d, 1H, $J_{1,2}$=4.88 Hz, H-1), 5.03-4.43 (m, 10 H, $C_6H_5C\underline{H}_2$), 4.35-3.40 (m, 12H), 1.48-1,33 (12H, C ($C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D3β** δ 138.6-127.4 (aromatic C), 109.5 ($\underline{C}_a(CH_3)_2$), 108.7 ($\underline{C}_b(CH_3)_2$), 102.3 (C-1'), 96.4 (C-1), 81.9, 75.8, 75.1, 74.8, 73.6, 73.4, 72.7, 71.6, 71.0, 70.8, 70.5, 69.9, 69.5, 68.1, 26.03, 25.97, 25.1, and 24.4 ($C(\underline{C}H_3)_2$), $[\alpha]_D^{22}$-48.5 (*c* 1.23, $CHCl_3$).

Ethyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-*N*-phthalimido-1-thio-β-D-glucopyranoside (D4α). Glycosidation of **1** (147.6 mg) with **8** (68.7 mg) using IDCP yielded D4α. Chromatography gave pure **D4α** (145 mg, 96%), while glycosidation of **1** (63.3 mg) with **8** (39.8 mg) using DMTST yielded **D4α**, which was flash chromatographed to give pure **D4α** (31.5 mg, 36%) : R_f 0.43 for **1**, 0.07 for **8**, 0.32 for **D4α** (toluene-EtOAc, 15 : 1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74-6.92 (m, 29H, aromatic H), 5.55 (s, 1H, C_6H_5CH), 5.48 (d, 1H, $J_{1,2}$=10.72 Hz, H-1), 5.32 (d, 1H, $J_{1',2'}$=1.96 Hz, H-1'), 4.78-4.17 (m, 11H), 3.91-3.68 (m, 5H), 3.61 (dd, 1H, *J*=3.16 Hz, 9.52 Hz), 3.02 (m, 2H), 2.80 (m, 1H), 2.68 (m, 2H, SCH_2CH_3), 1.19 (t, 3H, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8 and 167.3 (CO), 138.9-123.2 (aromatic C), 101.8 (C_6H_5CH), 98.8 (C-1'), 82.7 (C-4), 81.9 (C-1), 79.5 (C-3'), 74.9, 74.7, 74.3, 73.8, 73.3, 72.8, 72.1, 71.8, 70.2, 68.7 and 67.8 (C-6 and C-6'), 54.2 (C-2), 24.2 (SCH_2CH_3), 14.9 (SCH_2CH_3), $[\alpha]_D^{24}$+11.3 (*c* 0.51, $CHCl_3$).

Methyl *O*-(2,4,6-tri-*O*-benzyl-3-*O*-*p*-methoxybenzyl-α-D-mannopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D5α) and methyl *O*-(2,4,6-tri-O-benzyl-3-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D5β). Glycosidation of **2** (74.3 mg) with **6** (30 mg) using IDCP yielded a mixture. Flash chromatography gave **D5α** (45.7 mg, 61%) and **D5β** (20.8 mg, 28%) while glycosidation of **2** (233.7 mg) with **6** (107.8 mg) using MeOTf yielded a mixture, which was flash chromatographed to give **D5α** (100.6 mg, 38%) and **D5β** (28.2 mg, 11%) : R_f 0.68 for **2**, 0.22 for **6**, 0.54 for **D5α**, and 0.38 for **D5β** (toluene-EtOAc, 5 : 1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D5α** δ 7.47-7.06 (m, 27H, aromatic H), 6.80 (d, 2H, *J*=8.52 Hz, $CH_3OC_6H_4$ aromatic H), 5.48-5.47 (m, 2H), 4.90-4.22 (m, 13H), 4.08-4.07 (m, 2H), 3.87-3.60 (m, 9H), 3.51 (t, 1H), 3.42-3.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D5α** δ 158.9-113.6 (aromatic C), 101.8 (C_6H_5CH), 98.8 (C-1), 97.7 (C-1'), 82.7, 79.3, 77.9, 74.8, 74.6, 74.1, 73.6, 73.5, 73.2, 71.6, 71.4, 71.3, 69.1 and 68.9 (C-6 and C-6'), 61.8 (C-5), 55.3 and 55.2 (OCH_3 and $CH_3OC_6H_4$); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D5β** δ 7.48-7.16 (m, 27 H, aromatic H), 6.81 (d, 2 H, *J*=8.8 Hz, $CH_3OC_6H_4$ aromatic H), 5.50 (s, 1H, C_6H_5 CH), 4.95-4.36 (m, 13H), 4.24-4.16 (m, 2H), 3.91 (t, 1H), 3.83-3.60 (m, 8H), 3.51 (dd, 1H), 3.38-3.36 (m, 4H), 3.31-3.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D5β** δ 159.0-113.7 (aromatic C), 101.9 (C_6H_5CH), 101.4(C-1'), 98.5 (C-1), 82.3, 80.1, 76.0, 75.1, 74.8, 74.7, 73.8, 73.6, 73.3, 71.4, 69.4 and 68.9 (C-6 and C-6'), 62.5 (C-5), 55.3 and 55.2 (OCH_3 and $CH_3OC_6H_4$), $[\alpha]_D^{24}$+9.75 (*c* 0.79, $CHCl_3$).

Methyl *O*-(2,4,6-tri-*O*-benzyl-3-*O*-*p*-methoxybenzyl-α-D-mannopyranosyl)-(1→3)-4,6-*O*-benzylidene-α-D-galactopyranoside (D6α-3) and methyl *O*-(2,4,6-tri-*O*-benzyl-3-*O*-*p*-methoxybenzyl-α-D-mannopyranosyl)-(1→2)-4,6-*O*-benzylidene-α-D-galactopyranoside (D6α-2). Glycosidation of **2** (278.4 mg) with **10** (116.3 mg) using IDCP yielded a mixture. Flash chromatography gave **D6α-3** (123.8 mg, 36%) and **D6α-2** (99.7 mg, 29%) : R_f 0.85 for **2**, 0.02 for **10**, 0.39 for **D6α-3**, and 0.3 for **D6α-2** (toluene-EtOAc, 5 : 3); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D6α-3** δ 7.48-6.78 (m, aromatic H), 5.53 (s, 1H, C_6H_5CH), 5.03-3.54(m, 22H), 3.79 (s, 3H, $CH_3OC_6H_4$), 3.34 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D6α-3** δ 159.1-113.7 (aromatic C), 101.1 (C_6H_5CH), 98.5 and 97.6 (C-1 and C-1'), 79.4, 76.3, 75.3, 75.0, 74.5, 73.1, 73.0, 72.3, 71.8, 69.2, 69.0, 67.4, 62.5, 55.5 and 55.2 (OCH_3 and $CH_3OC_6H_4$), $[\alpha]_D^{22}$+44.6 (*c* 2.28, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D6α-2** δ 7.46-7.10 (m, 22H, aromatic H), 6.81 (d, 2H, *J*= 8.52 Hz, $CH_3OC_6H_4$ aromatic H), 5.43 (s, 1H, C_6H_5CH), 5.03 (d, 1H, $J_{1',2'}$=1.44 Hz, H-1'), 4.88 (d, 1H, $J_{1,2}$=3.64 Hz, H-1), 4.83-4.25 (m, 9H, $C_6H_5CH_2$, $CH_3OC_6H_4CH_2$ and 1H), 4.17 (d, 1H, *J*=3.4 Hz), 4.09-3.79 (m, 7H), 3.77 (s, 3H, $CH_3OC_6H_4$), 3.74-3.68 (m, 2H), 3.59 (s, 1H), 3.37 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D6α-2** δ 159.1-113.7 (aromatic C), 100.7 (C_6H_5CH), 100.3 (C-1), 95.3 (C-1'), 79.5, 75.1, 75.0, 74.5, 73.4, 73.3, 72.9, 72.8, 72.1, 71.8, 69.5, 69.4, 67.2, 62.4, 55.6 and 55.2 (OCH_3 and $CH_3OC_6H_4$), $[\alpha]_D^{24}$+ 90.1 (*c* 1.93, $CHCl_3$).

Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (D7β). Glycosidation of **3** (73.6 mg) with **5** (79 mg) using IDCP yielded a mixture. Flash chromatography gave **D7β** (16 mg, 12%) : R_f 0.68 for **3**, 0.11 for **5**, and 0.41 for **D7β** (toluene-EtOAc, 5 : 1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D7α** δ 7.51-7.16 (m, 30H, aromatic H), 5.59 (s, 1H, C_6H_5CH), 5.04-4.49 (m, 11H), 4.27-3.69 (m, 8H), 3.53-3.43 (m, 4H), 3.33 (s, 3H, OCH_3), 3.25-3.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D7β** δ 138.8-126.0 (aromatic C), 102.0 (C_6H_5CH), 101.4 (C-1'), 97.8 (C-1), 82.2, 79.8, 78.6, 77.8, 77.2, 75.7, 75.6, 74.7, 74.5, 73.3, 72.5, 69.6, 68.5, 68.2, 67.5, 55.1 (OCH_3), $[\alpha]_D^{24}$-2.07 (*c* 1.99, $CHCl_3$), ES(+)MS [100, $(M+NH_4)^+$].

Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D8β). Glycosidation of **3** (182.6 mg) with **6** (91.2 mg) using IDCP yielded a mixture. Flash chromatography gave **D8β** (20.3 mg, 10%) : R_f 0.7 for **3**, 0.22 for **6**, and 0.32 for **D8β** (toluene-EtOAc, 5 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D8β** δ 7.52-7.18 (m, 30H, aromatic H), 5.53 (m, 2H, C_6H_5CH), 4.90 (s, 1H), 4.72-3.47 (m, 18H), 3.35 (s, 3H, OCH_3), 3.25-3.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D8β** δ 159.1-113.7 (aromatic C), 103.0 (C-1'), 101.3 and 101.1 (C_6H_5CH), 98.5 (C-1), 80.0, 79.9, 79.2, 78.8, 78.7, and 78.2 (C-2, 2', 3, 3', 4, and 4'), 74.5, 73.4, and 72.5 ($C_6H_5CH_2$), 68.9, 68.7, 67.3, and 62.5 (C-5, 5', 6, and 6'), 55.3 (OCH_3), $[\alpha]_D^{24}$-3.04 (*c* 0.73, $CHCl_3$).

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (D9α) and 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (D9β). Glycosidation of **3** (284.9 mg) with **7** (136.9 mg) using MeOTf yielded a mixture. Flash chromatography gave **D9α** (61.9 mg, 17%) and **D9β** (147.3 mg, 41%) : R_f 0.66 for **3**, 0.07 for **7**, 0.40 for **D9α** (toluene-EtOAc, 5 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D9α** δ 7.51-7.23 (m, 15H, aromatic H), 5.63-5.51 (m, 2H, H-1, C_6H_5CH), 4.49-4.58 (m, 6H), 4.32-4.16 (m, 4H), 3.98-3.66 (m, 7H), 1.52-1.31 (m, 12H, $C(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D9α** δ 138.7-126.0 (aromatic C), 109.4 ($C_8(CH_3)_2$), 108.6 ($C_8(CH_3)_2$), 101.4 (C_6H_5CH), 99.0(C-1'), 96.3 (C-1), 79.0 (C-4'), 76.4 (C-2' and C-3'), 74.3 and 73.1 ($C_6H_5CH_2$), 70.9, 70.6, 70.5 (C-2, C-3, C-5) 68.8, 65.8, 65.4, 64.4 (C-4, C-6, C-5', C-6'), 26.1, 25.9, 24.9, and 24.5 ($C(CH_3)_2$), $[\alpha]_D^{22}$-6.09 (*c* 0.88, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D9β** δ 7.52-7.16 (m, 15H,

aromatic H), 5.60-5.58 (m, 2H), 5.01-4.53 (m, 6H), 4.34-3.37 (m, 11H), 1.53-1.31 (m, 12H, C($C\underline{H}_3$)$_2$);e ^{13}C NMR ($CDCl_3$, 100 MHz) for **D9β** δ 138.2-125.9 (aromatic C), 109.3 ($\underline{C}_a(CH_3)_2$), 108.5 ($\underline{C}_b(CH_3)_2$), 102.7 (C-1'), 101.2 ($C_6H_5\underline{C}H$), 96.2 (C-1), 78.3, 77.3, 74.8, 74.4, 71.9, 71.4, 70.6, 70.4, 69.9, 68.4, 67.8, 67.4, 25.9, 25.8, 24.9, and 24.2 (C($\underline{C}H_3$)$_2$), $[\alpha]_D^{22}$-78.0 (*c* 2.29, $CHCl_3$).

Methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-α-D-mannopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (D10α) and methyl O-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (D10β). Glycosidation of **4** (150.5 mg) with **5** (111.5 mg) using DMTST yielded a mixture. Flash chromatography gave **D10α** (14.9 mg, 7%) and **D10β** (105.6 mg, 48%) : R_f 0.68 for **4**, 0.11 for **5**, 0.53 for **D10α**, and 0.41 for **D10β** (toluene-EtOAc, 5 : 1, v/v); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D10α** δ 159.1-113.7 (aromatic C), 101.5 ($C_6H_5\underline{C}H$), 99.6 (C-1'), 97.8 (C-1), 82.1, 80.1, 79.1, 77.7, 76.3, 75.8, 75.4, 75.0, 73.4, 73.3, 72.6, 69.8, 68.8, 66.0, 64.3, 55.2 and 55.0 ($O\underline{C}H_3$ and $\underline{C}H_3OC_6H_4$), $[\alpha]_D^{24}$+43.6 (*c* 0.41, $CHCl_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D10β** δ 159.2-113.7 (aromatic C), 101.9 ($C_6H_5\underline{C}H$), 101.3 (C-1'), 97.8 (C-1), 82.1, 79.7, 78.6, 77.4, 75.65, 75.6, 74.6, 74.4, 73.3, 72.1, 69.6, 68.5, 68.2, 67.5, 55.2 and 55.0 ($O\underline{C}H_3$ and $\underline{C}H_3OC_6H_4$).

Methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-α-D-mannopyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D11α) and methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (D11β). Glycosidation of **4** (140.2 mg) with **9** (83.2 mg) using DMTST yielded a mixture. Flash chromatography gave a mixture (102.6 mg, 55%) of **D11α** and **D11β** (1 : 2.5) : R_f 0.68 for **4**, 0.18 for **9**, 0.51 for a mixture of **D11α** and **D11β** (toluene-EtOAc, 5 : 1); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D11α** δ 159.0-113.6 (aromatic C), 101.4 and 101.3 ($C_6H_5\underline{C}H$), 96.9 (C-1'), 96.2 (C-1), 81.9, 76.1, 75.5, 75.47, 73.9, 73.5, 72.8, 68.9, 68.5, 64.2, 62.3, 55.2 and 55.1 ($O\underline{C}H_3$ and $\underline{C}H_3OC_6H_4$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D11β** δ 159.1-113.6 (aromatic C), 103.0 (C-1'), 101.4 and 101.3 ($C_6H_5\underline{C}H$), 100.3 (C-1), 82.6, 78.9, 78.4, 78.1, and 78.0 (C-2, 2', 3, 4, and 4'), 75.2, 75.1, 74.3, and 72.1 (C-3', $C_6H_5\underline{C}H_2$, and $CH_3OC_6H_4\underline{C}H_2$), 69.1, 68.4, 67.5 and 62.3 (C-5, 5', 6, and 6'), 55.4 and 55.2 ($O\underline{C}H_3$ and $\underline{C}H_3OC_6H_4$).

1,2:3,4-Di-*O*-isopropylidene-6-*O*-*p*-methoxybenzyl-α-D-galactopyranose (12). Glycosidation of **4** (406.9 mg) with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (7) (184.2 mg) using MeOTf yielded a mixture. Fash chromatography gave **12** (207.5 mg, 41%) while glycosidation of **4** (191.9 mg) with **7** (85.7 mg) using DMTST yielded a mixture, which was flash chromatographed to give **12** (34.5 mg, 15%) : R_f 0.69 for **4**, 0.07 for **7**, 0.43 for **12** (toluene-EtOAc, 5 : 1); ^{13}C NMR ($CDCl_3$, 100 MHz) for **12** δ 159.1-113.5 (aromatic C), 109.1 ($\underline{C}_a(CH_3)_2$), 108.4 ($\underline{C}_b(CH_3)_2$), 96.3 (C-1), 71.1 (C-5), 70.53 (C-2), 70.48 (C-3), 68.4 (C-4), 66.8 (C-6), 26.0, 25.9, 24.9, and 24.4 (C($\underline{C}H_3$)$_2$).

Methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→3)-4,6-*O*-benzylidene-α-D-galactopyranoside (D13β-3) and methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→2)-4,6-*O*-benzylidene-α-D-galactopyranoside (D13β-2). Glycosidation of **4** (159.2 mg) with **10** (77.1 mg) using MeOTf yielded a mixture. Flash chromatography gave **D13β-3** (60.7 mg, 30%) and **D13β-2** (65.4 mg, 32%) while glycosidation of **4** (512.4 mg) with **10** (193.3 mg) using DMTST yielded a mixture, which was flash chromatographed to give **D13β-3** (122.9 mg, 24%) and **D13β-2** (118.6 mg, 23%) : R_f 0.77 for **4**, 0.05 for **10**, 0.52 for **D13β-3**, and 0.36 for **D13β-2** (toluene-EtOAc, 5 : 3); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D13α-3** δ 7.52-7.18 (m, 17 H, aromatic H), 6.82 (d, 2 H, *J*=8.52 Hz, $CH_3OC_6H_4$ aromatic H), 5.59 and 5.57 (both s, 1H each, $C_6H_5\underline{C}H$), 5.00-3.53 (m, 18H), 3.79 and 3.43 (doth s, 3H each, $\underline{C}H_3OC_6H_4$ and OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D13β-3** δ 159.1-113.7 (aromatic C), 103.2 (C-1'), 101.4 and 101.3 ($C_6H_5\underline{C}H$), 100.4 (C-1), 78.4, 77.5, 77.2, 76.3, 75.6, 74.6, 71.9, 69.4, 68.6, 68.5 67.6, 62.3, 55.8 and 55.3 (OCH_3 and $\underline{C}H_3OC_6H_4$); ^{1}H NMR ($CDCl_3$, 400 MHz) for **D13β-2** δ 7.54-7.15 (m, 17H, aromatic H), 6.82 (d, 2 H, *J*=8.76 Hz, $CH_3OC_6H_4$ aromatic H), 5.60 and 5.56 (both s, 1H each, $C_6H_5\underline{C}H$), 5.01-3.31 (m, 18H), 3.79 and 3.48 (both s, OCH_3 and $\underline{C}H_3OC_6H_4$); ^{13}C NMR ($CDCl_3$, 100 MHz) for **D13β-2** δ 159.1-113.6 (aromatic C), 103.0 (C-1'), 101.4 and 100.7 ($C_6H_5\underline{C}H$), 100.2 (C-1), 78.4, 77.5, 76.4, 75.8, 75.4, 74.5, 71.9, 69.1, 68.9, 68.5, 67.7, 63.1, 55.6 and 55.2 ($O\underline{C}H_3$ and $\underline{C}H_3OC_6H_4$).

Methyl *O*-(α-D-mannopyranosyl)-(1→6)-α-D-glucopyranoside (D1'α).[4] Compound **D1α** (50.9 mg) was hydrogenated in EtOAc (2 mL)-EtOH (4 mL) in the presence of 10% Pd/C for 24 hours at room temperature. Filtration over Celite pad and concentration of the filtrate yielded **D1'α** quantitatively : R_f 0.47 for **D1'α** (t-BuOH-EtOAc-HAc-H_2O, 36 : 36 : 7 : 21, v/v); ^{1}H NMR (D_2O, 400 MHz) for **D1'α** δ 4.68 (s, 1H, H-1'), 4.59 (s, 1H, H-1); ^{13}C NMR (D_2O, 100 MHz) for **D1'α** δ 100.5 (C-1'), 100.4 (C-1), 74.3, 73.7, 72.2 (C-2), 71.6, 70.9, 70.8, 70.4, 67.7, 66.2 (C-6), 61.9 (C-6'), 56.0 (OCH_3), $[\alpha]_D^{24}$+92.7 (*c* 0.47, H_2O).

Methyl *O*-(β-D-mannopyranosyl)-(1→6)-α-D-glucopyranoside (D1'β).[4] Hydrogenation of compound **D1β** (37.6 mg), as described for the preparation of **D1'α**, yielded **D1'β** quantitatively : R_f 0.40 for **D1'b** (t-BuOH-EtOAc-HAc-H_2O, 36 : 36 : 7 : 21, v/v); ^{1}H NMR (D_2O, 400 MHz) for **D1'β** δ 4.59 (d, 1H, $J_{1,2}$=3.68 Hz, H-1), 4.48 (s, 1H, H-1'); ^{13}C NMR (D_2O, 100 MHz) for **D1'β** δ 101.5 (C-1'), 100.3 (C-1), 77.3, 74.0, 73.9, 72.1, 71.6, 71.4, 70.5, 69.2 (C-6), 67.8, 62.0 (C-6'), 56.1 (OCH_3), $[\alpha]_D^{24}$+52.0 (*c* 0.35, H_2O).

Results and Discussion

Reactions of perbenzyl ethylthio β-D-gluco or galactopyranoside in the presence of IDCP were reported to give stereoselectively 1,2-*cis*-α-glycosides *via* inversion at C-1.[7,9,16] Our study with perbenzylated ethylthio-α-D-mannopyranoside (**1**) shows preferential formation of α-D-mannosyl disaccharides (Table 1, entry 1-8), in variable α/β-anomeric ratios depending on acceptors, promoters, and solvents. It is noteworthy that unlike glucose or galactose derivatives,[18] retention at C-1 occurred preferentially in reactions of perbenzylated ethylthio-α-D-mannopyranoside (**1**), giving thermodynamically stable α-mannopyranosides (1,2-trans-glycosides) in major.[9,14] α-Anomeric ratios increased with the steric hindrance of accepter-OH, but were affected little by promoters. Employing IDCP promoter **1** was coupled to

accepters **5** (6-OH), **6** (3-OH), **7** (hindered 6-OH), and **8** (3-OH) in α/β ratios of 1.5/1, 4.7/1, 3/1, and 1/0, respectively (entry 1, 5-7). Solvent polarity influenced the stereochemical outcome of mannose-coupling and the efficiency also. Comparison of entries, 1 with 2, and 3 with 4, shows that addition of ether to CH_2Cl_2 (CH_2Cl_2 : Et_2O=2 : 5) increased coupling yields (53 to 78 and 72 to 84%) and α/β ratios (1/1 to 1.5/1 and 1.35/1 to 1.5/1, respectively).

IDCP is proved to be the most efficient promoter in terms of yields, reaction time and manageability. With IDCP promoter α-D-mannosyl-disaccharide (**D4α**) was obtained in 96% yield from coupling of perbenzyl ethylthio-α-D-mannopyranoside (**1**) and ethyl 4,6-*O*-benzylidene-2-deoxy-2-*N*-phthalimido-1-thio-β-D-glucopyranoside (**8**) (entry 7) while with DMTST in 36% yield. DMTST probably attacked thioglycoside **1** and **8** indiscriminately. Thus, DMTST is less effective than IDCP as a promoter for armed-disarmed coupling of thio-glycosides (entry 7, 8). IDCP was compatible with the presence of 4-methoxyphenylmethyl (MPM) ether, while MeOTf or DMTST were not. With IDCP coupling of ethyl 2,4,6-tri-*O*-benzyl-3-*O*-MPM-1-thio-α-D-mannopyranoside (**2**) to methyl 4,6-*O*-benzylidene-2-*O*-benzyl-α-D-glucopyranoside (**6**) produced **D2** (Man3Glc) in 89% yield (entry 9), whereas the same coupling with MeOTf gave **D2α** (Man3Glc) in only 49% yield (entry 10). MeOTf gave no disaccharides but a very little 6-*O*-MPM-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**12**) from the reaction of **2** with 1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (**7**) (entry 11). Sequential reactions of MPM-ether cleavage and intermolecular MPM migration must have occurred by MeOTf.

In coupling of donor **2** to methyl 4,6-*O*-benzylidene-α-D-galactopyranoside (**10**) by IDCP the contrast with its β-anomeric accepter is remarkable in regioselectivity for its 2-OH and 3-OH. Only (1→3) linked disaccharide between donor **2** and methyl 4,6-*O*-benzylidene-β-D-galactopyranoside acceptor (the β-anomer of acceptor **10**) was reported[17] while coupling of donor **2** with **10** produced Manα3Gal (**D6α-3**) and Manα2Gal (**D6α-2**) in 36 and 29% yields (entry 12). The axial α-OCH_3 of **10** appears to hinder its 3-OH sterically and thus reduce its regioselectivity.

Anomeric assignments of mannosyl disaccharides are based on ^1H and ^{13}C NMR data (Table 2) together with their specific rotations. C-1 chemical shift values of α-mannosyl disaccharides are lower than those of their β-anomers and specific rotations of the former are more bigger than those of the latter.[4,19,20]

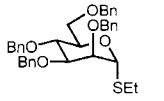
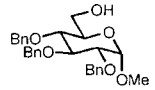
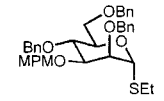
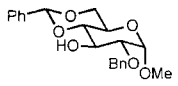
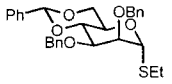
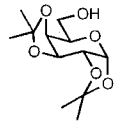
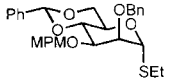
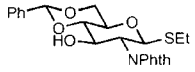
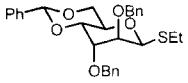
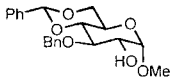
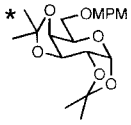
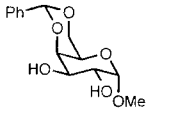
IDCP was not so efficient as MeOTf or DMTST in activating

Table 2. ^{13}C NMR data for mannosyl disaccharides (δ in ppm) in $CDCl_3$

	D1α	D1β	D2α	D2β	D3α	D3β	D4α
C-1	97.7	97.7	98.7	98.5	96.3	96.4	81.9
C-1'	98.1	101.4	97.6	101.4	97.2	102.3	98.8
	D5α	**D5β**	**D6α-3**	**D6α-2**	**D7β**	**D8β**	**D9α**
C-1	98.8	98.5	98.5	100.3	97.8	98.5	96.3
C-1'	97.7	101.4	97.6	95.3	101.4	103.0	99.0
	D9β	**D10α**	**D10β**	**D11α**	**D11β**	**D13β-3**	**D13β-2**
C-1	96.2	97.8	97.8	96.2	100.3	100.3	100.2
C-1'	102.7	99.6	101.3	96.9	103.0	103.1	103.0

C-1' denotes for the mannosyl anomeric carbon.

Figure 1. List of compounds

No.	Donor	No.	Acceptor
1		5	
2		6	
3		7	
4		8	
11		9	
12		10	

bicyclic mannosyl donors such as ethyl 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside (**3**) (entries 13 and 14) and ethyl 4,6-*O*-benzylidene-2-*O*-benzyl-3-*O*-MPM-1-thio-α-D-mannopyranoside (**4**) (entries 17, 20 and 21) donors, resulting in poor yields or no coupling at all. However coupling of **3** and **7** (entry 15), **4** and **5** (entry 16), and **4** and **9** (entry 22) using MeOTf or DMTST produced mannosyl disaccharides Man6Gal in 57%, Man6Glc in 55%, and Man2Glc in 55% yield, respectively. It is also of interest to note β-D-mannosyl disaccharides,[21-24] hardly obtainable by chemical syntheses,[25-28] were formed preferentially in coupling of benzylidenated mannosyl donors **3** or **4**.[29] Entries 15, 16, and 22 showed the produce of Man6Gal, Man6Glc, and Man2Glc in α/β ratios of 1/2.4, 1/7.1 and 1/2.5, respectively. More about the preferential formation of β-D-mannosyl disaccharides from benzylidenated mannosyl donors will be reported elsewhere. Similar results were reported by Crich and Sun.[19-20,30] Decomposition of MPM-ether by MeOTf or DMTST was more evident with donor **4**. In coupling of **4** and **7**, 1,2:3,4-di-*O*-isopropylidene-6-*O*-MPM-α-D-galactopyranose (**12**) was isolated in 41 and 15% yield (entries 18, 19) as a result of MPM migration of donor **4** to acceptor **7**.

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Ozonolyses of Cycloalkenes: Trapping of Carbonyl Oxide by Trifluoroacetophenone

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Ozonolysis reactions of cyclic olefins **1a-c** and norbornene **1n** in the presence of trifluoroactophenone **6** provided the corresponding cross-ozonides **7a-c** and **7n**. Further reactions of ozonides **7a-c** and **7n** with the independently prepared carbonyl oxide **11** gave diozonides of structure **10a-c** and **10n**. The ozonolysis of 1-methylcyclopentene **12a** and 1-methylcyclohexene **12b** in the presence of trifluoroactophenone **6** provided exclusively ozonide **15** and **16** derived from capture of carbonyl oxide **13**. All of the new ozonides have been isolated as pure substances and characterized by their ^{1}H NMR and ^{13}C NMR spectra.

Introduction

Ozonolyses of cycloalkenes in aprotic solvents result in formation of polymeric peroxides, because of the intramolecular cycloaddition of carbonyl oxide with aldehyde is much slower than that of intramolecular process.[1-3]

Ozonolyses of certain cycloolefins **1** in methanol, however, revealed a partially anomalous behavior as compared to acyclic olefins. A priori, one would have expected that the primary intermediates of type **2** are trapped by methanol to give compounds of type **4**. But in addition to **4**, variable amounts of the isomeric product of type **5** were obtained.[4,5]