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Brønsted Acids of Anionic Chiral Cobalt(III) Complexes as Catalysts for the Iodoglycosylation or Iodocarboxylation of Glycals

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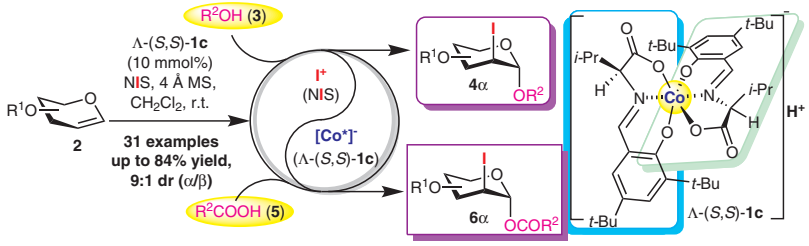

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Abstract Brønsted acids of anionic chiral Co(III) complexes were found to act as efficient phase-transfer catalysts for the diastereoselective iodoglycosylation or iodocarboxylation of glycals with a variety of alcohols or carboxylic acids, respectively, with *N*-iodosuccinimide as the iodo cation source. The corresponding 2-deoxy-2-iodoglycosides, including monosaccharides and disaccharides, and 2-deoxy-2-iodoglycosyl carboxylates, which are of high synthetic and biological importance, were obtained in high yields (up to 88%) with good diastereoselectivities (up to 9:1 dr).

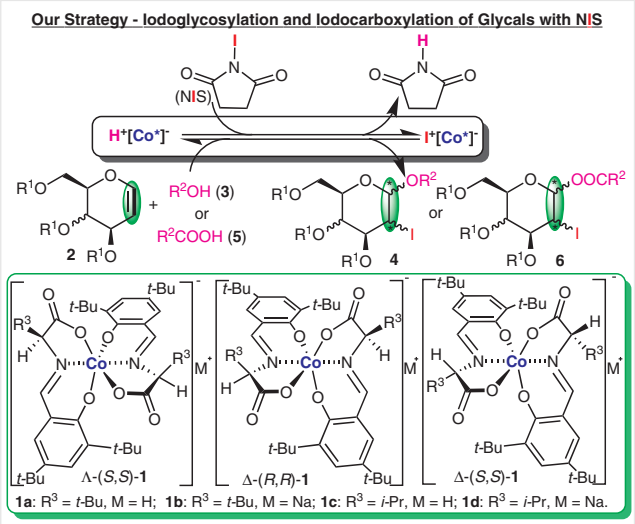
Key words Brønsted acids, phase-transfer catalysis, iodoglycosylation, iodocarboxylation, glycals

Mono- and oligosaccharides are prevalent motifs in biologically active natural products such as glycopeptides, glycoproteins, proteoglycans, and glycolipids.[1] Deoxy sugars also constitute key intermediates with widespread applications in medicinal and pharmaceutical research.[2] Therefore, the development of efficient methods for the synthesis of these glycomolecules in high stereoselectivity and with broad structural diversity is undoubtedly appealing in chemistry, biology, and related fields.[2f,3] Remarkable progress has been made, especially in transition-metal-catalyzed and organocatalyzed conventional glycosylations for the preparation of complex carbohydrates.[4] In this study, we focused on the iodoglycosylation and iodocarboxylation of glycals by using anionic chiral Co(III) complexes as phase-transfer catalysts, affording the corresponding 2-deoxy-2-iodoglycosides and 2-deoxy-2-iodoglycosyl carboxylates, which are of high synthetic and biological importance.[5] Although iodoglycosylations and iodoacetoxylations through stoichiometric glycosylations using glycals and alcohols or acetic acid in the presence of an electrophilic iodine reagent (NIS) or an iodate reagent such as NH_4I, NaI, I_2, or $TMSI(OAc)_2$ with an oxidant [for example, H_2O_2, CAN, $Cu(OAc)_2$, $PhI(OAc)_2$,[6] PPh_3,[6h] or TfOH[5d]] have been reported, the exploration of high-performance catalytic systems that are, in principle, distinct from previous ones remains essential for the development of mild and efficient stereoselective glycosylation methods. Furthermore, there are few reports on the catalytic stereocontrol of such reactions with chiral catalysts, due to the difficulty of asymmetric intermolecular halogenation[7,8] or glycosylation.[4,9]

The potential of the octahedral chiral-at-metal complexes, in which the metal center does not serve as a catalytic center to activate substrate by coordination but merely provides a rigid framework and an environment of centrochirality, is less well recognized.[10] We have recently developed Brønsted acids and sodium salts of anionic chiral Co(III) complexes as efficient catalysts for the highly enantioselective bromoaminocyclization of olefins and for the Povarov reaction of enol ethers with 2-azadienes.[11] More importantly, the chiral Co(III)-complex-templated Brønsted acids have been proved to function as bifunctional phase-transfer catalysts to shuttle *N*-bromosuccinimide (NBS) to the reaction solution and to control stereoselectivity.[11c,d] We therefore speculated that such anionic chiral Co(III) complexes might also serve as alternative chiral-anion-mediated catalysts[12] with an iodo-cation source for the iodoglycosylation[4,6a,13] of glycals **2**[14] with alcohols **3** or carboxylic acids **5** (Scheme 1).

Here, we present our preliminary studies on catalytic iodoglycosylation and iodocarboxylation reactions for the preparation of 2-deoxy-2-iodoglycosides **4** and 2-deoxy-2-iodoglycosyl carboxylates **6** by using anionic chiral Co(III) complexes **1**.

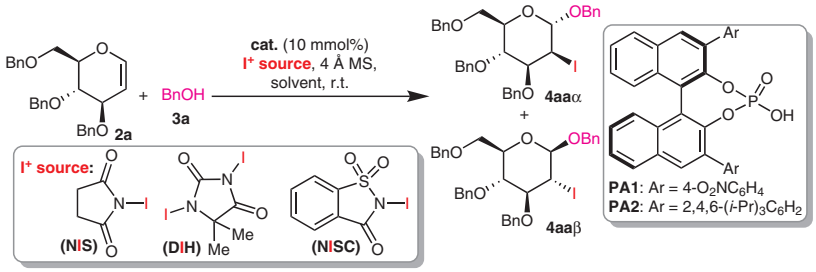
The diastereoselective iodoglycosylation of 3,4,6-tri-*O*-benzyl-D-glucal (**2a**) and benzyl alcohol (**3a**) with NIS at room temperature was initially tested, and the corresponding 2-deoxy-2-iodoglycoside **4aa** was obtained in 69% yield



Scheme 1 Chiral Co(III)-complex-templated phase-transfer catalysis

with a 2:1 dr (α/β ratio) without a catalyst (Table 1, entry 1). As expected, the reaction occurred smoothly in the presence of various Lewis acids (entries 2–9), delivering the product in good yields (up to 86%), albeit with only up to 2.5:1 dr, even at a low temperature of –40 °C (entries 6 and 8).[5d] Several Brønsted acids, such as *p*-toluenesulfonic acid and the chiral phosphoric acids **PA1** and **PA2**, were also tested, and the results suggested that the proton has no impact on the diastereoselectivity (entries 10–12). When DMAP and PPh_3 were employed as the catalysts, the α/β ratio of **4aa** was only 3:1 (entries 13 and 14). A series of anionic chiral Co(III) complexes, either as sodium salts or Brønsted acids, were then screened (entries 15–21), Λ-(*S*,*S*)-**1c** afforded the best diastereomeric ratio of 4:1 in the highest yield of 86% (entry 18). The metal-centered chirality in the chiral Co(III)-complex-templated Brønsted acids had little effect on the stereochemical outcome of the iodoglycosylation (entries 16, 19, and 20). Several iodinating reagents, such as 1,3-diiodo-5,5-dimethylhydantoin (DIH) and *N*-iodosaccharine (NISC), were then tested, and NIS was found to be the optimal iodine source for this protocol (entries 18, 22, and 23). To our delight, changing the ratio of **2a**, **3a**, and NIS ratio slightly improved the diastereoselectivity (entry 24). Moreover, a screening of the reaction parameters, including the solvent, temperature, and additives, suggested that the reaction in CH_2Cl_2 at room temperature gave a higher α/β ratio of 5:1 with 4 Å MS (entries 24–34).

Table 1 Optimization of the Conditions for Iodoglycosylation[a]



Entry	Catalyst	Solvent	I+ source	Yield[b] (%)	dr[c] (α/β)
1	–	CH_2Cl_2	NIS	69	2:1
2[d]	$ZnBr_2$	CH_2Cl_2	NIS	76	1.5:1
3[d]	$Sc(OTf)_3$	CH_2Cl_2	NIS	86	1:1
4[d]	$Mg(OTf)_2$	CH_2Cl_2	NIS	85	1.6:1
5[d]	TMSOTf	CH_2Cl_2	NIS	78	1.5:1
6[d,e]	TMSOTf	CH_2Cl_2	NIS	55	2:1
7[d]	TfOH	CH_2Cl_2	NIS	59	1.8:1
8[d,e]	TfOH	CH_2Cl_2	NIS	45	2.5:1
9[d]	AgOTf	CH_2Cl_2	NIS	50	2.5:1
10[d]	$TsOH·H_2O$	CH_2Cl_2	NIS	69	1.5:1
11	**PA1**	CH_2Cl_2	NIS	61	2:1
12	**PA2**	CH_2Cl_2	NIS	51	2:1
13[d]	DMAP	CH_2Cl_2	NIS	54	3:1

Table 1 (continued)

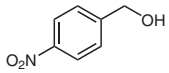
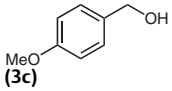
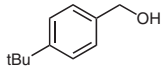
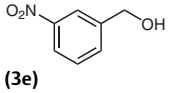
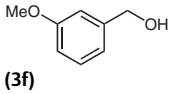
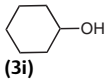
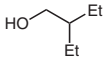
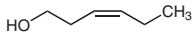
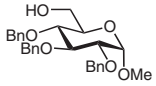
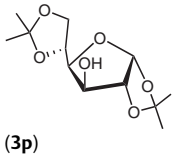
Entry	Catalyst	Solvent	I^+ source	Yield[b] (%)	dr[c] (α/β)
14[d,e]	PPh_3	CH_2Cl_2	NIS	85	3:1
15	Λ-(*S*,*S*)-**1a**	CH_2Cl_2	NIS	82	3:1
16	Δ-(*R*,*R*)-**1a**	CH_2Cl_2	NIS	85	3.5:1
17	Λ-(*S*,*S*)-**1b**	CH_2Cl_2	NIS	56	3.8:1
18	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	86	4:1
19	Δ-(*R*,*R*)-**1c**	CH_2Cl_2	NIS	78	3.5:1
20	Δ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	50	2:1
21	Λ-(*S*,*S*)-**1d**	CH_2Cl_2	NIS	79	3:1
22	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	DIH	40	3:1
23	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NISC	12	3:1
24[f]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	82	5:1
25[f]	Λ-(*S*,*S*)-**1c**	CCl_4	NIS	74	3.5:1
26[f]	Λ-(*S*,*S*)-**1c**	$CHCl_3$	NIS	85	3.8:1
27[f]	Λ-(*S*,*S*)-**1c**	DCE	NIS	79	4.5:1
28[f]	Λ-(*S*,*S*)-**1c**	toluene	NIS	76	3:1
29[f,g]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	51	4:1
30[f,h]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	74	4.5:1
31[f,i]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	60	3:1
32[f,j]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	80	4:1
33[f,k]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	79	4:1
34[f,l]	Λ-(*S*,*S*)-**1c**	CH_2Cl_2	NIS	64	4:1

[a] Unless otherwise noted, the reaction was performed with glycal **2a** (0.1 mmol), **3a** (0.15 mmol), NIS (0.12 mmol), catalyst (0.01 mmol), 4 Å MS (100 mg) in the solvent (1 mL) at r.t. under N_2 in the absence of light for 24 h.
[b] Yield of isolated product **4aa**.
[c] Determined by ^{1}H NMR.
[d] Catalyst (20 mmol%) was used.
[e] The reaction was carried out at –40 °C.
[f] The **2a**/**3a**/NIS ratio was 1:1.2:1.1.
[g] The reaction was carried out at 35 °C.
[h] The reaction was carried out at 0 °C.
[i] The reaction was carried out at –20 °C.
[j] 3 Å MS (100 mg) was used instead of 4 Å MS.
[k] 5 Å MS (100 mg) was used instead of 4 Å MS.
[l] No additive was used.

With the optimized reaction conditions in hand,[15] we next explored the scope of the iodoglycosylation with respect to the alcohol **3**. As shown in Table 2, various substituents on the aryl moiety of the benzyl alcohols **3b–f** were tolerated, affording the corresponding 2-deoxy-2-iodoglycosides **4** in up to 73% yield with up to 4.5:1 dr (Table 2, entries 1–5). The electronic nature of the substrates had no evident influence on the reactivity. In addition, 1-naphthylmethanol was also well tolerated and provided the product **4ag** with 4:1 dr (entry 6). Nonbenzylic aliphatic alcohols **3h–n** were also suitable substrates, giving the desired glycosides **4ah–an** in high yields and up to 6.5:1 dr (entries 7–13). Sterically hindered alcohols **3j** and **3k** readily participated in the reaction with up to 6.5:1 dr (entries 9 and 10). The *Z*-alkene in **3n** was also well tolerated (4:1 dr; entry 13). More importantly, the iodoglycosylation proceeded under mild conditions with monosaccharides such as the primary alcohol **3o** and the secondary alcohol **3p**, giving the corresponding disaccharides with up to 9:1 dr (entries 14 and 15).

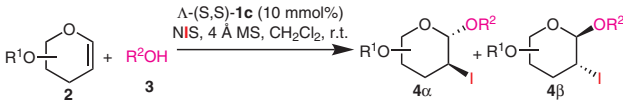
The scope of the iodoglycosylation using Brønsted acid of anionic chiral Co(III)-complexes **1** with regard to the glycals **2** was also evaluated (Table 3). Glycals with other hydroxy-protecting groups, such as **2b** and **2c**, were good substrates for the iodoglycosylation reaction, giving the corresponding products in moderate to high yields and with up to 8:1 dr (entries 1–8). Moreover, tri-*O*-benzyl-D-galactal (**2d**), the C4-epimer of **2a**, afforded the corresponding products in moderate yields with similar diastereoselectivities (up to 6.5:1 dr; entries 9 and 10).[16]

Table 2 Scope of the Alcohols **3** for the Iodoglycosylation[a]

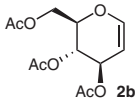
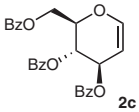
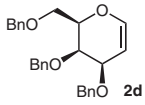
Entry	Alcohol	Product	Yield[b] (%)	dr[c] (α/β)	dr[d] (Lit.)
1	 **(3b)**	**4ab**	72	4:1	–
2	 **(3c)**	**4ac**	62	4.5:1	–
3	 **(3d)**	**4ad**	73	4:1	–
4	 **(3e)**	**4ae**	56	4:1	–
5	 **(3f)**	**4af**	66	4.5:1	–
6	CyOH **(3g)**	**4ag**	75	4:1	–
7	$Ph(CH_2)_2OH$ (**3h**)	**4ah**	84	4.5:1	–
8	 **(3i)**	**4ai**	78	4.5:1	4.8:1[6h]
9	*i*-PrOH (**3j**)	**4aj**	73	5:1	2:1[6h]
10	*t*-BuOH (**3k**)	**4ak**	72	6.5:1	–
11	$Me(CH_2)_7OH$ (**3l**)	**4al**	78	4:1	2.3:1[6h]
12	 (**3m**)	**4am**	78	4:1	–
13	 (**3n**)	**4an**	76	4:1	–
14[e]	 (**3o**)	**4ao**	88	6.5:1	2.5:1[6h]
15[e]	 (**3p**)	**4ap**	53	9:1	–

[a] Unless otherwise noted, the reaction was performed with glycal **2a** (0.1 mmol), alcohol **3** (0.12 mmol), NIS (0.11 mmol), Λ-(*S*,*S*)-**1c** (0.01 mmol), and 4 Å MS (100 mg) in CH_2Cl_2 (1 mL) at r.t., under N_2 in the absence of light for 24 h.
[b] Yield of isolated product.
[c] Determined by ^1H NMR.
[d] Anomer ratios reported in the literature.
[e] The reaction was carried out on a 0.1 mmol scale for 72 h with a **2a**/**3**/NIS ratio of 2:1:2.4.

Table 3 The Scope of Glycals for the Iodoglycosylation[a]



2 3 4α 4β

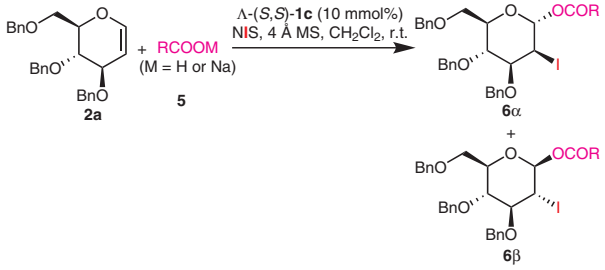
Entry	Glycal	Alcohol	Product	Yield[b] (%)	dr[c] (α/β)	dr[d] (Lit.)
1	 2b	**3a**	**4ba**	80	8:1	5:1[6d] 9:1[6e]
2		**3c**	**4bc**	54	5:1	–
3		**3f**	**4bf**	55	4:1	6:1[6d] 11:1[6e]
4		**3g**	**4bg**	70	5:1	–
5		**3h**	**4bh**	63	4.5:1	–
6	 2c	**3a**	**4ca**	60	4:1	–
7		**3c**	**4cc**	66	5:1	–
8		**3j**	**4cj**	61	5:1	–
9	 2d	**3c**	**4dc**	47	4:1	–
10		**3k**	**4dk**	52	6.5:1	–

[a] Unless otherwise noted, the reaction was performed with glycal **2** (0.1 mmol), alcohol **3** (0.2 mmol), NIS (0.15 mmol), Λ-(*S*,*S*)-**1c** (0.01 mmol), and 4 Å MS (100 mg) in CH_2Cl_2 (1 mL) at r.t. under N_2 in the absence of light for 48 h.
[b] Yield of isolated product.
[c] Determined by ^{1}H NMR.
[d] Anomer ratios reported in the literature.

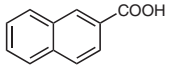
Encouraged by these results, we next studied the iodocarboxylation of glycal **2a** with carboxylic acids and sodium salts **5** to give the corresponding 2-deoxy-2-iodoglycosyl carboxylates **6** (Table 4).[17] The reaction of the sodium salts **5a** and **5c** and the acids **5b** and **5d** in the absence of the chiral-Co(III)-complex-templated Brønsted acid were first tested, and products **6a** and **6b** were obtained with low diastereoselectivities (Table 4, entries 1-4). Interestingly, the presence of the Brønsted acid of a chiral Co(III) complex Λ-**1c** resulted in enhanced diastereoselectivity (up to 6.5:1 dr; entries 5–8), but the sodium salts of the acids still gave low yields (entries 5 and 6). It is suggested that the presence of an acidic proton might promote the reaction and that the bulky chiral Co(III) complexes influence the stereocontrol. The protocol also tolerated other carboxylic acids, and the corresponding glycosyl carboxylates **6c–e** were obtained with good diastereoselectivities (up to 7.5:1 dr; entries 9–11).

Next, we performed a ^{1}H NMR spectral analysis of mixtures of NIS with Brønsted acid Λ-(*S*,*S*)-**1c** or benzoic acid (**5b**) in $CDCl_3$ at room temperature. The presence of succinimide in the former mixture clearly revealed that Λ-(*S*,*S*)-**1c** reacted with NIS to produce a new complex,[11c,d] thereby leading to the formation of succinimide, while no evidence was found to show that there is an interaction between benzoic acid (**5b**) and NIS in the latter mixture (Figure 1).

Table 4 The scope of the Iodocarboxylation[a]



2a 5 6α 6β

Entry	Acid or Na Salt	Product	Catalyst	Yield[b] (%)	dr[c]
1	BzONa (**5a**)	**6a**	–	14	3.5:1
2	BzOH (**5b**)	**6a**	–	82	2:1
3	AcONa (**5c**)	**6b**	–	29	2.5:1
4	AcOH (**5d**)	**6b**	–	70	1.8:1
5	BzONa (**5a**)	**6a**	Λ-(*S*,*S*)-**1c**	28	3.8:1
6	AcONa (**5c**)	**6b**	Λ-(*S*,*S*)-**1c**	28	5.5:1
7	BzOH (**5b**)	**6a**	Λ-(*S*,*S*)-**1c**	74	6.5:1
8	AcOH (**5d**)	**6b**	Λ-(*S*,*S*)-**1c**	65	5.5:1[d]
9	4-$F_3CC_6H_4CO_2H$ (**5e**)	**6c**	Λ-(*S*,*S*)-**1c**	67	6:1
10	 (**5f**)	**6d**	Λ-(*S*,*S*)-**1c**	62	6:1
11	2,6-$Cl_2C_6H_4CO_2H$ (**5g**)	**6e**	Λ-(*S*,*S*)-**1c**	75	7.5:1

[a] Unless otherwise noted, the reaction was performed with glycal **2a** (0.1 mmol), **5** (0.15 mmol), NIS (0.12 mmol), Λ-(*S*,*S*)-**1c** (0.01 mmol), and 4 Å MS (100 mg) in CH_2Cl_2 (1 mL) at r.t. under N_2 in the absence of light for 12 h.
[b] Yield of isolated product.
[c] Determined by ^{1}H NMR.
[d] The reported anomer ratio of **5d** was 4:1.[6f]

On the basis of the interesting experimental results and our previous work,[11c,d] we propose a plausible mechanism for these reaction of a chiral-Co(III)-templated Brønsted acid in combination with NIS. As shown in Scheme 2, the Brønsted acid **1** might undergo an exchange reaction with NIS to generate a reactive chiral iodinating reagent **7**, as suggested by the ^{1}H NMR spectral analysis. The chiral ion-pair **7** might then undergo diastereoselective reaction with the glycal **2** to afford the 2-deoxy-2-iodoglycoside **4** or a 2-deoxy-2-iodoglycosyl carboxylate **6** through nucleophilic addition of the alcohol **3** or carboxylic acid **5**, respectively, with regeneration of Brønsted acid **1**. The stereochemical outcomes were not good enough to have been caused by the competition of the rapid noncatalytic reaction of NIS.

In summary, we have developed a diastereoselective iodoglycosylation or iodocarboxylation of glycals with NIS mediated by a chiral-Co(III)-complex-templated Brønsted acid. The catalytic reaction proceeds under mild conditions, providing convenient access to 2-deoxy-2-iodoglycosides or 2-deoxy-2-iodoglycosyl carboxylates in up to 88% yield and with up to 9:1 dr. The anionic chiral Co(III) complexes also

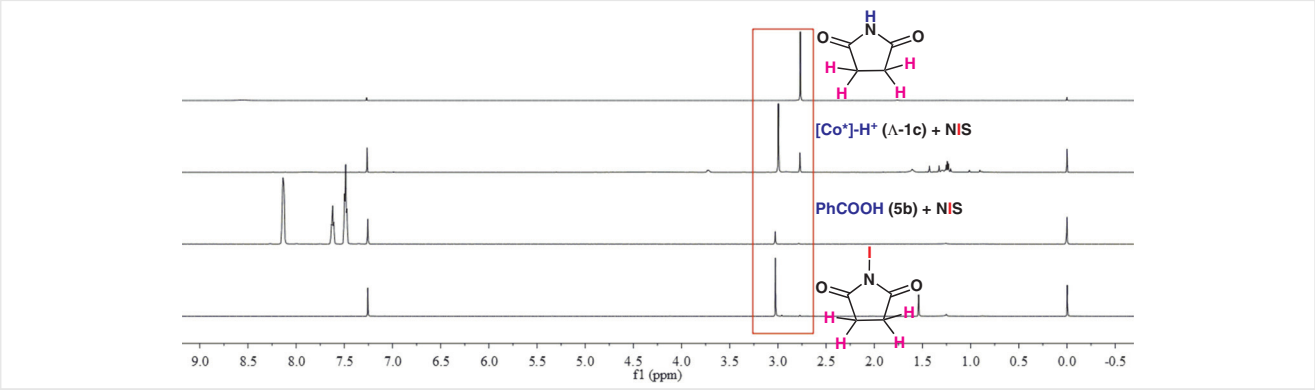
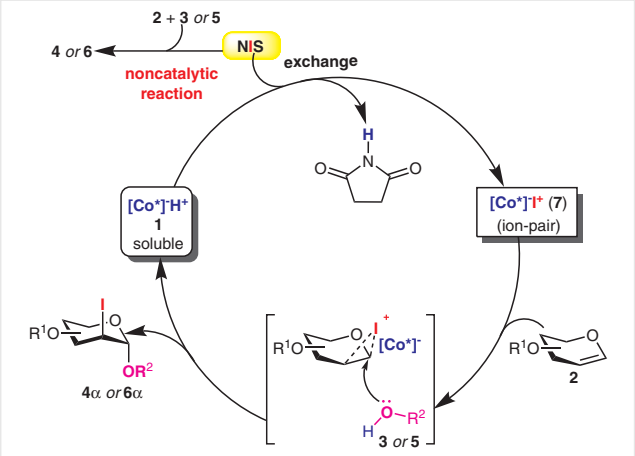


Figure 1 ^{1}H NMR analysis of mixtures of NIS with Brønsted acid Λ-(*S*,*S*)-**1c** or benzoic acid (**5b**) in $CDCl_3$.



Scheme 2 Proposed mechanism

function as bifunctional phase-transfer catalysts to shuttle the *N*-iodosuccinimide to the reaction solution. Further studies will focus on the development of stereoselective halogenations catalyzed by Brønsted acids of anionic chiral Co(III) complexes.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611810.

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(15) **2-Deoxy-2-Iodoglycoside 4aa; Typical Procedure**

A 10-mL oven-dried vial was charged with catalyst Λ-**1c** (7.2 mg, 0.01 mmol), NIS (24.8 mg, 0.11 mmol), activated 4 Å MS (100 mg), glycal **2a** (41.6 mg, 0.10 mmol), and distilled CH_2Cl_2 (1 mL) at r.t. in the absence of light. Alcohol **3a** (0.12 mmol) was added and the resulting solution was stirred vigorously under N_2 for 24 h. The reaction was then quenched with Et_3N (140 μL, 1.0 mmol) and sat. aq $Na_2S_2O_3$ (0.2 mL). The mixture was purified by flash column chromatography to give the 2-deoxy-2-iodoglycosides **4aa** as an α/β mixture.

4aaα

Colorless oil; yield: 43.9 mg (67%); R_f = 0.43 (PE–EtOAc, 10:1); $[\alpha]_D^{20}$ +3.45 (*c* 1.27, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.48–7.35 (m, 4 H), 7.35–7.19 (m, 14 H), 7.16 (d, *J* = 6.2 Hz, 2 H), 5.30 (s, 1 H), 4.84 (d, *J* = 10.8 Hz, 1 H), 4.72–4.66 (m, 3 H), 4.52–4.46 (m, 5 H), 3.92–3.91 (m, 2 H), 3.80–3.75 (m, 1 H), 3.69 (d, *J* = 10.8 Hz, 1 H), 3.37–3.34 (m, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 138.46, 138.29, 137.80, 136.98, 128.51, 128.44, 128.35, 128.10, 128.08, 128.05, 127.82, 127.69, 127.52, 100.85, 100.80, 76.05, 75.31, 73.47, 72.51, 71.04, 69.54, 69.00, 33.58, 33.55. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{34}H_{35}NaIO_5$: 673.1427; found: 673.1420.

4aaβ

White solid; yield: 9.5 mg (15%); mp 101–103 °C; R_f = 0.38 (PE–EtOAc, 10:1); $[\alpha]_D^{20}$ +4.91 (*c* 0.55, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.47–7.36 (m, 4 H), 7.36–7.26 (m, 14 H), 7.19 (d, *J* = 6.9 Hz, 2 H), 4.97 (d, *J* = 10.2 Hz, 1 H), 4.92 (d, *J* = 11.7 Hz, 1 H), 4.85 (d, *J* = 10.1 Hz, 1 H), 4.80 (d, *J* = 10.9 Hz, 1 H), 4.68 (d, *J* = 11.8 Hz, 1 H), 4.62 (t, *J* = 9.6 Hz, 2 H), 4.57 (t, *J* = 12.5 Hz, 2 H), 4.01–3.94 (m, 1 H), 3.77–3.70 (m, 3 H), 3.64 (t, *J* = 9.2 Hz, 1 H), 3.49 (d, *J* = 7.6 Hz, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 138.17, 137.90, 137.85, 136.88, 128.55, 128.48, 128.42, 128.33, 128.18, 127.98, 127.89, 127.83, 127.76, 101.98, 86.01, 79.79, 75.62, 75.42, 75.03, 73.65, 71.39, 68.72, 32.68. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{34}H_{35}NaIO_5$: 673.1427; found: 673.1422. (see Supporting Information for further information).

(16) Iodoglycosylations of either glucal (**2b**) or galactal (**2d**) with alcohol **3c** in the absence of the chiral-Co^{III}-complex-templated Brønsted acid were also tested, affording the desired 2-deoxy-2-iodoglycosides in yields of 52% and 24% with 2.5:1 and 1.8:1 dr, respectively.

(17) **2-Deoxy-2-Iodoglycosyl Carboxylate 6a; Typical Procedure**

A 10-mL oven-dried vial was charged with catalyst Λ-**1c** (7.2 mg, 0.01 mmol), NIS (27.0 mg, 0.12 mmol), activated 4 Å MS (100 mg), glycal **2a** (41.6 mg, 0.10 mmol), and distilled CH_2Cl_2 (1 mL) at r.t. in the absence of light. BzOH (**5a**; 0.15 mmol) was added and the resulting solution was stirred vigorously under N_2 for 12 h. The reaction was then quenched with Et_3N (140 μL, 1.0 mmol) and sat. aq $Na_2S_2O_3$ (0.2 mL). The mixture was purified by flash column chromatography to give the glycosyl carboxylate **6a** as a α/β mixture.

6aα

Colorless oil; yield: 42.7 mg (64%); R_f = 0.4 (PE–EtOAc, 8:1); $[\alpha]_D^{20}$ +3.78 (*c* 0.82, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.0 Hz, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.41–7.35 (m, 4 H), 7.34–7.24 (m, 9 H), 7.22–7.16 (m, 2 H), 6.66 (s, 1 H), 4.90 (d, *J* = 10.5 Hz, 1 H), 4.76–4.72 (m, 2 H), 4.58–4.52 (m, 4 H), 4.13–4.09 (m, 1 H), 4.07–4.03 (m, 1 H), 3.83 (dd, *J* = 11.3, 4.0 Hz, 1 H), 3.71 (dd, *J* = 11.3, 1.6 Hz, 1 H), 3.33 (dd, *J* = 8.7, 4.1 Hz, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.07, 138.37, 138.08, 137.26, 133.75, 129.92, 129.12, 128.62, 128.57, 128.49, 128.38, 128.34, 128.32, 128.11, 127.94, 127.81, 127.59, 96.17, 76.20, 75.63, 75.31, 73.67, 71.22, 68.65, 31.20. HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_{34}H_{33}INaO_6$: 687.1220; found: 687.1215.

6aβ

Colorless oil; yield: 6.5 mg (10%); R_f = 0.4 (PE–EtOAc, 8:1); $[\alpha]_D^{20}$ +65.61 (*c* 0.22, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.7 Hz, 2 H), 7.60 (t, *J* = 7.3 Hz, 1 H), 7.47 (t, *J* = 7.7 Hz, 2 H), 7.43 (d, *J* = 7.4 Hz, 2 H), 7.36 (t, *J* = 7.3 Hz, 2 H), 7.34–7.23 (m, 9 H), 7.17 (d, *J* = 7.4 Hz, 2 H), 6.05 (d, *J* = 9.5 Hz, 1 H), 5.00 (d, *J* = 10.2 Hz, 1 H), 4.91 (d, *J* = 10.2 Hz, 1 H), 4.82 (d, *J* = 10.8 Hz, 1 H), 4.60 (dd, *J* = 15.7, 11.5 Hz, 2 H), 4.48 (d, *J* = 12.1 Hz, 1 H), 4.19 (t, *J* = 9.8 Hz, 1 H), 3.87–3.69 (m, 5 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.67, 137.76, 133.75, 130.34, 128.56, 128.51, 128.45, 128.16, 128.01, 127.98, 127.86, 127.80, 95.09, 85.65, 79.07, 76.17, 75.76, 75.10, 73.71, 68.02, 30.23. HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_{34}H_{33}INaO_6$: 687.1220; found: 687.1217. (See Supporting Information for further information).