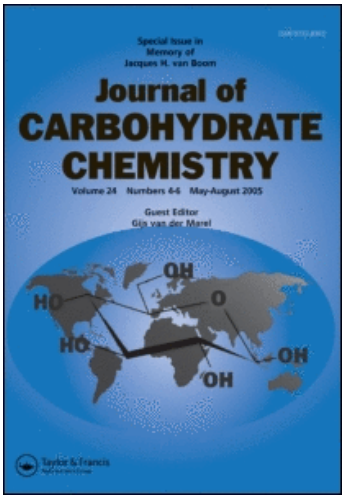

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Indium(III) Triflate: A Highly Efficient Catalyst for Reactions of Sugars[1]

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Indium(III) Triflate: A Highly Efficient Catalyst for Reactions of Sugars[1]

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Indium(III) trifluoromethanesulfonate has been found to be extremely efficient in catalyzing acyl transfer reactions of various carbohydrates and their derivatives. Selective acetolyses of certain benzyl ethers/isopropylidene acetals of sugars have been possible using $In(OTf)_3$ in Ac_2O (neat). Reaction of the per-*O*-acetate of 2-deoxy-2-phthalimido-D-glucose with benzyl mercaptan in the presence of $In(OTf)_3$ led to the formation of the corresponding thioglycoside in high yield. Facile formation and hydrolysis of the isopropylidene and benzylidene acetals of various carbohydrates have also been achieved very efficiently in the presence of $In(OTf)_3$. The results show great promise for $In(OTf)_3$ in synthetic carbohydrate chemistry.

Keywords Indium(III) triflate, acyl transfer reactions, acetal formation and hydrolysis, thioglycosylation

INTRODUCTION

A wide variety of Lewis acids have been in use for organic syntheses. Most of the classical reagents of this class, such as $AlCl_3$, $BF_3/BF_3.Et_2O$, $FeCl_3$, $SnCl_4$, $TiCl_4$, and $ZnCl_2$, are extremely sensitive to moisture and are difficult to handle, besides the fact that they are often required in stoichiometric quantities for the reaction to be highly effective. Among the more recently introduced metal-based Lewis acid substances, indium(III) salts have attracted a great deal of interest, particularly for their good stability in air and water.[2,3] Among the various In-based reagents, In(III) triflate has emerged as a useful catalyst in many organic transformations[2–4] including, for

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example, tetrahydropyranylation of alcohols,[5] Friedel-Crafts acylation of alcohols and amines,[6,7] Friedel-Crafts sulfonylation of arenes,[8] and ring opening of aziridines.[9] However, apart from an observation on the acetylation of an alditol using $Ac_2O/In(OTf)_3$[6] in MeCN, to the best of our knowledge no work has been reported in the literature on the use of this reagent in the area of synthetic carbohydrate chemistry. Therefore, an investigation was carried out in order to explore its possible applications in reactions of sugars and the results are reported herein.[10]

RESULTS AND DISCUSSION

Per-O-acetylation

Both the ability of the metal center in the In-based reagents to coordinate with electron-rich centers in organic molecules and the solubility of $In(OTf)_3$ in organic solvents must be of advantage in acyl transfer reactions using Ac_2O as the acyl donor reagent (Fig. 1).

Indeed, when D-galactose (**1**) was added to a solution of $In(OTf)_3$ in Ac_2O, the sugar went into solution within 10 sec and TLC at this stage revealed the formation of galactose pentaacetate (**2**, entry 1, Table 1). The reaction was considerably exothermic and no unreacted galactose or partially acetylated product could be detected in the reaction mixture. Aqueous workup yielded a solid product identical to authentic **2** by TLC and NMR and as observed in the case of acetylations catalyzed by other Lewis acids,[11,12] the α-anomer was preferentially formed.

Reaction of D-mannose (**3**) proceeded even faster under these conditions and the penta-*O*-acetate **4** (entry 2, Table 1) was obtained in very few seconds. Acetylation of the monosaccharide **5** and the disaccharides **7**, **9**, and **11** also took place in a very short period of time, giving the respective fully acetylated products in quantitative yields (Table 1, entries 3 and 5–7, respectively).

Peracetylation of the reducing disaccharides containing 1,2-*cis*- as well as 1,2-*trans*-configured interglycosidic linkages could thus be carried out without affecting such linkages, unlike in the case of instances under $FeCl_3$[11] catalysis. Acetylation of D-glucose (**5**) was then scaled up to 50 g without affecting the yield and portion-wise addition of glucose to the reaction

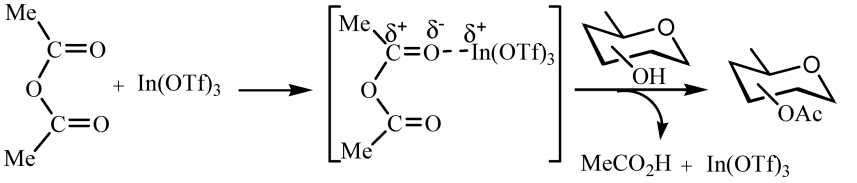
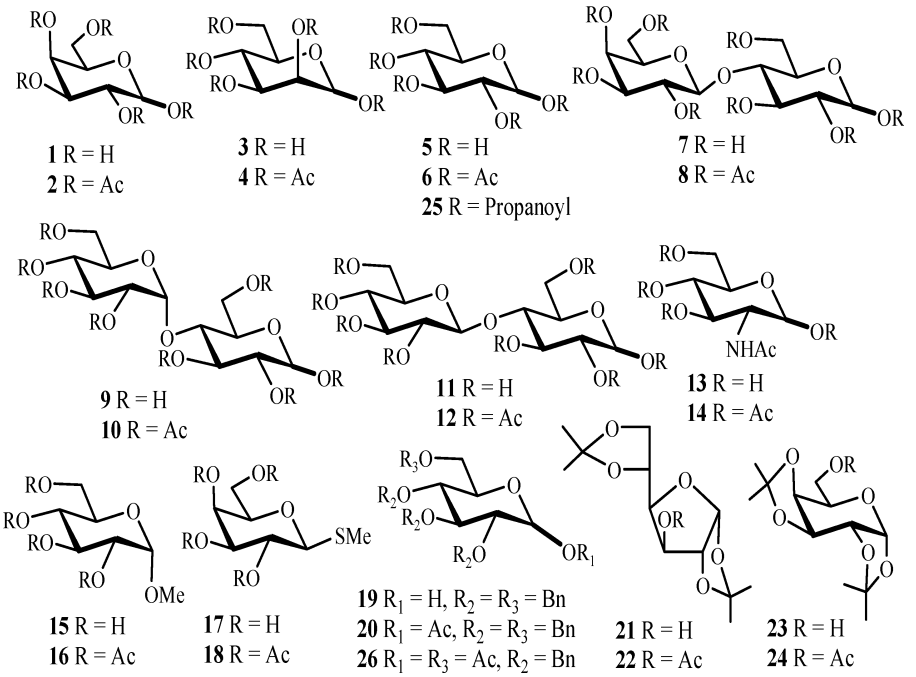


Figure 1: Proposed $In(OTf)_3$-promoted acetylation of sugers.



mixture was found necessary to avoid overheating of the reaction mixture (entry 4, Table 1). Acetylation of the acetamido derivative **13** was considerably slower than the parent sugar **5**, but the rate of *O*-acetylation could be increased by increasing the catalyst concentration (entries 8 and 9, Table 1).

Table 1: Indium(III) triflate-mediated acylation of sugars[a]

Entry	Sugar (quantity used)	$In(OTf)_3$ (mg/g sugar)	Reaction time	Product (yield, %; anomeric ratio, α:β)
1	**1**, 1 g	5	~10 sec	**2** (Quant; 9:2)
2	**3**, 1 g	5	A few sec	**4** (Quant; 7.7:1)
3	**5**, 1 g	5	3 min	**6** (Quant; 100:7)
4	50 g	2	30 min	**6** (Quant; 9:1)
5	**7**, 1 g	5	1 min	**8** (Quant; 9:1)
6	**9**, 1 g	5	A few sec	**10** (Quant; 3.7:1)
7	**11**, 1 g	5	5 min	**12** (Quant; 1:1)
8	**13**, 1 g	10	2 h	**14** (Quant; 1:1)
9	**13**, 1 g	50	0.5 h	**14** (Quant; 1:1)
10	**15**, 1 g	3.5	A few sec	**16** (Quant; —)
11	**17**, 0.21 g	1	1 min	**18** (90; —)
12	**19**, 0.54 g	1	1 min	**20** (93; 5.4:1)
13	**21**, 0.26 g	1	1 min at –15°C	**22** (93; —)
14	**23**, 0.26 g	1	1 min at -15 °C	**24** (92; —)
15	**5**, 1 g	5	2 h	**25** (90; 6:1)

[a]Acetylations were carried out using 5 mL Ac_2O/g sugar at rt or as specified; for propionylation 1.05 mol equiv. of propionic anhydride per OH group of the sugar was used at rt.

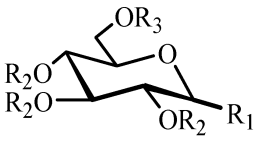
Thus, while at 0.32 mole% of $In(OTf)_3$ the reaction required 2 h at rt for the complete conversion of the amino sugar **13** to its peracetate **14**, the same transformation was complete in 30 min at 1.6 mole% concentration of the catalyst. It may be recalled that conversion of **13** to **14** required 2 days for completion when carried out using I_2 at a concentration of 17.7 mole% at rt.[12] Simple alkyl glycosides such as **15** also could be per-*O*-acetylated with ease on using approximately 0.11 mole% of the catalyst in Ac_2O at rt (entry 10, Table 1) without the aglycone group being affected. But with alkyl thioglycosides such as **17**, the amount of $In(OTf)_3$ had to be reduced to approximately one-third for the desired tetra-*O*-acetate **18** to be obtained without the loss of the aglycone moiety (entry 11, Table 1).

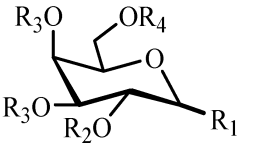
Not surprisingly though, it was also observed that further control of the rate of acylation (as well as avoidance of acetolysis) could be achieved by carrying out the reaction at –15°C instead of rt (see also later). These observations enabled successful acetylation of partially benzylated sugar derivative **19** (entry 12, Table 1) and acetonides **21** and **23** (entries 13 and 14, Table 1) in the cold by using the triflate reagent in as low a concentration as 0.03 to 0.06 mole%. The desired monoacetates (**20**, **22**, and **24**, respectively) were obtained in excellent yield in all three instances. The results of the foregoing experiments clearly show $In(OTf)_3$ to be a lot more of an effective catalyst than Lewis acids such as $FeCl_3$[11] and I_2[12] reported for this purpose. Possible involvement of the triflic acid/acetyl triflate that may be formed in situ in the reaction mixture, particularly subsequent to the onset of acetylation in the initial stages of the reaction, may also account for the enhanced rate of acyl transfer in the case of $In(OTf)_3$-catalyzed acetylation reactions reported here. Potential of this reagent for acylation reactions was further evaluated by using neat propionic anhydride as the acyl donor and **5** as the acyl acceptor (entry 15, Table 1). Excellent yield of the desired product **25** was obtained with ease.

Acetolysis

The potential of $In(OTf)_3$ for applications in acetolysis reaction was felt during the acetylation of the thioglycoside **17** as described above. Acetolysis reactions become of particular interest in synthetic carbohydrate chemistry when regioselective/chemoselective transformations become possible. With this in mind, taking compounds **17**, **19**, **21**, **27**, **29**, and **31** as substrates, the use of $In(OTf)_3$-Ac_2O system was further investigated for its possible applications in selective/controlled acetolyses (Table 2).

Thus, acetolysis of the methylthio group in thiogalactoside **17** could be easily carried out by treatment of **17** with the $In(OTf)_3$-Ac_2O system under mild conditions to give the pentaacetate **2** in quantitative yield (entry 1, Table 2). Similarly, treatment of tetra-*O*-benzyl glucopyranose (**19**) with the reagent system led first to the glycosyl acetate **20** and further to the exclusive





27 R_1 = β-SMe, R_2 = R_3 = Bn
28 R_1 = OAc, R_2 = Bn, R_3 = Ac
29 R_1 = β-SMe, R_2 = R_3 = R_4 = Bn
30 R_1 = OAc, R_2 = R_3 = Bn, R_4 = Ac
31 R_1 = β-OSE, R_2 = R_4 = Bn, R_3-R_3 = Me_2C
32 R_1 = β-OSE, R_2 = R_4 = Bn, R_3 = Ac
33 R_1 = β-OSE, R_2 = Bn, R_3 = R_4 = Ac

SE = 2-(Trimethylsilyl)ethyl

formation of the regioselectively acetolyzed 1,6-di-*O*-acetate **26** (entry 2, Table 2) in approximately 5 h. As has been observed in other instances,[12] the 2-*O*-, 3-*O*-, and 4-*O*-benzyl groups remained unaffected. The rate of acetolysis of the 6-*O*-benzyl ether could be significantly enhanced by increasing the triflate concentration in the reaction mixture as evident from the formation of the di-*O*-acetates **28** and **30** from the corresponding benzyl derivatives **27** and **29** (entries 4 and 5, Table 2). The 2-(trimethylsilyl)ethyl residue in the galactoside derivative **31**, susceptible to acetolysis by $BF_3 \cdot Et_2O$[13] (or $FeCl_3$)[14] in Ac_2O, could be successfully transformed into the 3,4-di-*O*-acetate **32** chemoselectively using $In(OTf)_3/Ac_2O$ at –15°C in 75% yield with the remaining product being the 3,4,6-tri-*O*-acetate **33**. It is interesting to note that acetolysis of the isopropylidene acetal preceded that of the 6-*O*-benzyl group in this compound.

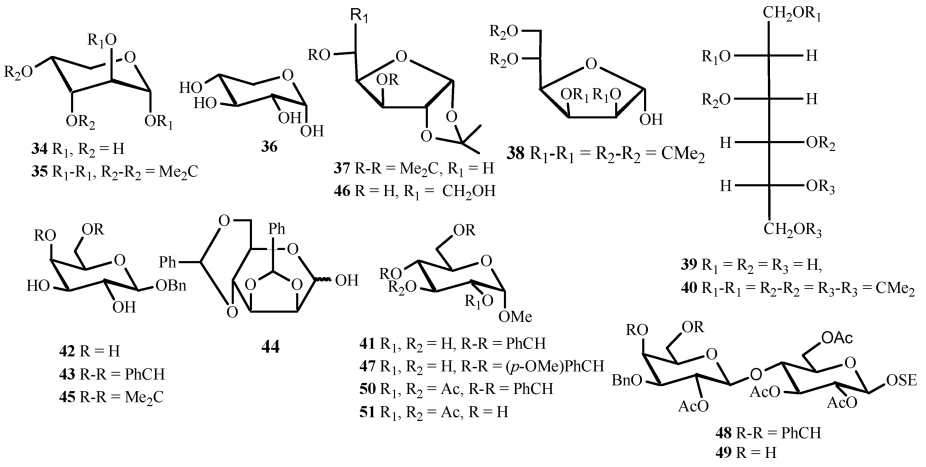
Formation and Hydrolysis of Acetals

Acetylation, in particular the preparation of isopropylidene as well as benzylidene acetals, is an extremely useful reaction in synthetic carbohydrate chemistry. In(III) halide-assisted thioacetalation reactions, including the transthioacetalation of cyclic/acyclic *O*,*O*-acetals of many noncarbohydrate

Table 2: Indium(III) triflate-mediated acetolysis of sugar derivatives[a]

Entry	Sugar	$In(OTf)_3$ (mg sugar) (mg sugar)	Reaction time	Product (yield, %)	α/β
1	**17** or **18**	5	1 min	**2**(98)	Neat α -
2	**19**	1	5 h	**26** (97)	4:1
3	**19**	5	1 min	**26** (97)	4:1
4	**27**	5	<1 min	**28** (92)	3.5:1
5	**29**	5	<1 min	**30** (92)	3:1
6	**31**	1	30 min at –15°C	**32** (75) **33** (25)	—

[a]Acetolyses were carried out using 1 mL Ac_2O/100 mg sugar derivative at rt or as specified.



substances as well as In(III) triflate-mediated conversion of aromatic/aliphatic carbonyl compounds to oxathiolanes by reaction with 2-mercaptoethanol, have been reported. In view of these facts, and in light of a recent report on the application of $V(OTf)_3$ in the preparation of sugar acetals, the reaction of acetone with simple aldoses in the presence of $In(OTf)_3$ was investigated (Table 3).

Typically, pentoses such as arabinose (**34**) and xylose (**36**) yielded their respective known di-*O*-isopropylidene derivatives **35** and **37**, respectively, in about 10 min at reflux temperature in the presence of 3.2 mole% of the catalyst

Table 3: Indium(III) triflate-mediated acetylation/transacetylation of sugars/their derivatives

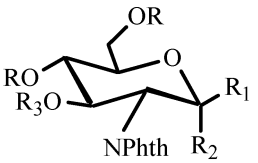
Entry	Sugar (wt)	Reaction time	Product	Yield, %
1[a]	**34** (1 g)	10 min	**35**	Quant.
2[a]	**36** (1 g)	10 min	**37**	Quant.
3[a]	**1** (1 g)	6 h	**23**	82
4[a]	**3** (1 g)	10 min	**38**	Quant.
5[a]	**5** (1 g)	8 h	**21**	90
6[b]	**5** (10 g)	12 h	**21**	91
7[a]	**39** (1 g)	10 min	**40**	Quant.
8[c]	**15** (1 g)	2 h	**41**	93
9[c]	**42** (1 g)	4 h	**43**	95
10[c]	**3** (1 g)	30 min	**44**	93
11[d]	**15**	2 min	**41**	83
12[d]	**42**	2 min	**43** (see entry 9)	97
13[e]	**42**	2 min	**45**	73

[a]0.032 mol equiv of $In(OTf)_3$ in 50 mL of acetone (HPLC grade) at reflux temperature was used.
[b]6.4×10^{-3} mol equiv of $In(OTf)_3$ in 200 mL of acetone (HPLC grade) at reflux temperature was used.
[c]0.25 mol equiv of $In(OTf)_3$ in PhCHO (neat, 5 mol equiv) at rt was used.
[d]15 mol equiv of $PhCH(OMe)_2$ (neat) and $In(OTf)_3$ (4 mg/100 mg sugar) were used at rt.
[e]15 mol equiv of $Me_2C(OMe)_2$ (neat) and $In(OTf)_3$ (4 mg/100 mg) were used at rt.

in acetone (entries 1 and 2, Table 3). In the case of hexoses, while D-galactose (**1**) and D-glucose (**5**) required 6 and 8 h, respectively, for the reaction (entries 3 and 5, Table 3), it was complete in 10 min in the case of D-mannose (**3**, entry 4, Table 3). D-Mannitol (**39**) also likewise gave the known tri-*O*-acetal **40** in 10 min at reflux temperature (entry 7, Table 3). Arabinose, xylose, mannose, and mannitol yielded the respective isopropylidene derivatives in quantitative yield, but the diacetonides of galactose and glucose were obtained in 82% and 90% yield, respectively (Table 3). The crude products obtained in all cases were pure enough for subsequent transformations.

Reaction of neat benzaldehyde with hexosides for the preparation of the respective 4,6-*O*-benzylidene acetals was subsequently investigated. Thus, the glucoside **15** and the galactoside **42** underwent facile acetylation reaction giving the respective 4,6-*O*-benzylidene acetals **41** and **43**, respectively, the isolated yields in both cases being more than 90% (entries 8 and 9, Table 3). Although the benzylidene acetals were indeed also obtained in the presence of solvents such as MeCN and DMF, it was noted that neat PhCHO best suited the purpose, as was revealed from the poorer yields (40%–60% only, results not shown) of these products obtained in the former. In neat reaction with PhCHO, D-mannose likewise gave the expected di-*O*-benzylidene acetal **44**, also in excellent yield (entry 10, Table 3). Transacetylations using the respective dimethylacetal derivatives of acetone/benzaldehyde as the carbonyl equivalents could also be carried out successfully (entries 11 and 12, Table 3) in the presence of $In(OTf)_3$.

Encouraged by the successful preparation of the acetals, the applicability of In(III) triflate in their hydrolysis was studied and the results are summarized in Table 4. The hydrolytic cleavage of acetals took place in a very facile manner when carried out at 50°C or 70°C in aq dioxane in the presence 10% (w/w) of the metal triflate.



52 R_1 = SMe, R_2 = H, R_3 = Bn, R-R = CMe_2
53 R_1 = SMe, R_2 = H, R_3 = Bn, R = H
54 R_1 = SMe, R_2 = H, R_3 = Bn, R = Ac
55 R_1= H, R_2 = OAc, R_3 = Ac, R = Ac
56 R_1= SBn, R_2 = H, R_3 = Ac, R = Ac

The diacetonide **21** underwent selective cleavage of the exocyclic acetal as expected giving the monoisopropylidene derivative **46** in good isolated yield. As to be expected, the reactions proceeded at a significantly faster rate at

Table 4: Indium(III) triflate-mediated hydrolysis of acetal derivatives of sugars[a]

Entry	Starting sugar	Temp (°C)	Time (h)	Product (yield, %)
1	**21**	50	2	**46** (71)
2	**21**	70	1	**46** (75)
3	**21**	70	10	**5** (85)
4	**47**	50	1.5	**15** (98)
5	**47**	70	0.5	**15** (98)
6	**48**	70	0.5	**49** (99)
7	**50**	70	3.5	**51** (90)
8	**52**	70	1.5	**53** (99)

[a]Reactions were carried out in aqueous dioxane (10%, (v/v) 1 mL/100 mg sugar) containing $In(OTf)_3$ (10% (w/w) sugar).

the higher temperature employed (Table 4). It may be emphasized that unlike in the case of the use of methanolic iodine,[15] for this category of reactions the present method is devoid of any risk of formation of methyl glycosides as by-products. Also, other acid-sensitive groups such as the 2-(trimethylsilyl)ethyl group (entry 6, Table 4) were stable and no loss of acetates or acetyl migrations were observed (see entries 6 and 7, Table 4). Stability of the glycosidic thiomethyl group as well as the phthalimido functionality under these hydrolytic conditions is evident from the high yield of the diol **53** obtained in the hydrolysis of the benzylidene derivative **52** (entry 8, Table 4). Compound **53** was further characterized as its corresponding acetate derivative, methyl 4,6-di-*O*-acetyl-3-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**54**).

Thioglycosylation

Potential for further use of this metal triflate was indicated when 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranose (**55**)[16] was treated with benzyl mercaptan (this particular thiol was chosen on account of its relatively high boiling point; it also facilitates the reaction monitoring by TLC using UV detection) in the presence of $In(OTf)_3$ at 40°C to 50°C whereby benzyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**56**)[17] was obtained in 96% isolated yield. The reaction could be facilitated successfully in the presence of one-fourth mol equiv of the triflate reagent (as compared to the glycosyl acetate substrate **55** used) in refluxing CH_2Cl_2 or in DCE at 50°C, and as to be expected the product was exclusively of 1,2-*trans*-cofiguration. Further work required in the optimization of the reaction conditions and to explore the applicability of the method in preparing various other thioglycosides are currently under way in our laboratory.

CONCLUSION

The use of indium(III) trifluoromethanesulfonate in various reactions (such as acetylation and acetolysis, formation and hydrolysis of cyclic *O*-acetals,

and thioglycosylation) of carbohydrates has been demonstrated in the present work.

ACKNOWLEDGMENTS

We would like to thank the Department of Science & Technology, New Delhi, India, for financial support.

EXPERIMENTAL

All reagents (Aldrich) were used as purchased without further purification. Reactions were monitored by TLC, which was performed with 0.2-mm Merck precoated silica gel 60 F254 aluminum sheets. Compounds were detected under UV light and by dipping the TLC plates in an ethanolic solution of sulphuric acid (4% v/v) followed by heating. Silica gel 60–120 mesh (Spectrochem Pvt. Ltd., India)/silica gel 200–400 mesh (SD Fine-Chem. Pvt. Ltd., India) was used for column chromatography. Hexane refers to a mixture of isomeric hexanes. Melting points (uncorrected) were determined on a Digital Melting Point Apparatus (Perfit, India). Optical rotations were recorded on a Rudolph AUTOPOL IV Polarimeter at approximately 24°C. ^{1}H NMR spectra were recorded at 300 MHz on a Bruker DPX300 spectrometer in deuteriochloroform. Chemical shifts are expressed relative to that of the residual proton in the deuterated solvents (δ 7.25). ^{13}C NMR spectra were recorded at 75.47 MHz. Assignments of resonances are based on published data. The anomeric ratios of products reported in the tables were determined from their NMR spectra. All the compounds, except **32**, reported here have been reported previously; many are commercially available and therefore analytical data for compound **32** only have been listed here. The physical constants obtained for the known compounds agreed with the literature data and their spectral data were in agreement with the values expected for their respective structures. Room temperature refers to approximately 30°C.

General Procedure for Acetylation/Acetolysis

The sugar (or its derivative) was suspended (or dissolved as the case is) in acetic anhydride (5 mL/g of sugar for acetylation and 10 mL/g of sugar for acetolysis, see Tables 1 and 2) and stirred. $In(OTf)_3$ (5 to 50 mg/g sugar or its derivative, see Tables 1 and 2) was added and stirring was continued until TLC showed the reaction to be complete. In small-scale reactions the reaction mixture was diluted with CH_2Cl_2 and was washed successively with aq Na_2CO_3 and water. The organic layer was then dried (Na_2SO_4) and concentrated to give the product. In large-scale acetylations the reaction mixture was poured into ice-cold dilute sodium carbonate solution with stirring. The products were allowed to crystallize in the refrigerator and were separated by filtration.

The products thus obtained were pure enough in most cases for use elsewhere directly or else were purified by column chromatography.

The following compounds were prepared:

Compounds **2**, **4**, **6**, **8**, **10**, **12**, **14**,[18,19] **16**,[20] **18**, **27**, **29**,[21] **20**[23] (from **19**[22]), **22**, **24**,[26] **25**,[27,28] **26**,[29] **28**, **30**,[12] **32**,[32] and **33**[33](from **31**[30,31]).

Typical Procedure for the Acetylation of D-Glucose

D-Glucose (**5**, 1g, 5.55 mmol) was taken in acetic anhydride (5 mL) and stirred at rt (32°C) after the addition of $In(OTf)_3$ (5 mg, 0.009 mmol). The immediate warming of the reaction mixture indicated the onset of acetylation and was soon led to the dissolution of the sugar indicating completion of the reaction, which was confirmed by TLC (EtOAc:*n*-Hex, 1:1, v/v) on comparison with authentic α-D-glucose penta-*O*-acetate. A colorless homogeneous reaction mixture was obtained within a few minutes. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and was poured into a beaker containing crushed ice followed by neutralization with aqueous Na_2CO_3. The product was extracted with CH_2Cl_2 (20 mL × 2), and the combined organic extracts were washed successively with aq Na_2CO_3 as well as brine, dried (Na_2SO_4), and concentrated under reduced pressure followed by crystallization (diethylether and petroleum ether, bp. 60–80°C). The product was obtained (2.1 g) as a colorless crystalline solid in quantitative yield.

In large-scale preparations (5–50 g or more), the sugar was added to the acid anhydride in portions and upon completion of the reaction, the mixture was directly poured into a beaker containing crushed ice, neutralized with aqueous Na_2CO_3, and left for a few hours in a fridge for crystallization. The resulting solids were filtered, washed with ice-cold water, and dried under reduced pressure. The product was obtained as white powder in quantitative yield.

Preparation of 28

$In(OTf)_3$ (5 mg, 0.009 mmol) was added to a stirred solution of 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**27**, 100 mg, 0.55mmol) in acetic anhydride (1.5 mL) at rt (32°C), and the stirring was continued until the reaction was complete by TLC (EtOAc:*n*−Hex, 1:2, v/v). Aqueous workup as discussed above yielded the desired product, 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl D-glucopyranoside (**28**, α:β, 3.5:1),[12] as a colorless crystalline solid (yield, 86 mg, 92%).

General Procedure for Acetylation/Transacetylation

To a mixture of the sugar/sugar derivative in acetone (HPLC grade) or neat $PhCHO/PhCH(OMe)_2/Me_2C(OMe)_2$, depending upon the reaction, $In(OTf)_3$

was added at the desired temperature and was stirred until TLC showed complete conversion. Aqueous workup yielded the products.

The following compounds were prepared:

Compounds **21**,[24,25] **23**,[24] **35**,[34] **37**,[35] **38**,[25] **40**,[36] **41**,[37] **43**,[38] **44**,[39] and **45**.[40]

Preparation of 21

$In(OTf)_3$ (100 mg, 0.18 mmol) was added to a suspension of D-Glucose (1.0 g, 5.55 mmol) in acetone (50 mL) at reflux temperature and stirring was continued until TLC (EtOAc:*n*-Hex, 1:1, v/v) showed complete conversion. No undissolved sugar was visible at this stage. Aqueous workup yielded crystalline 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**21**, 1.30 g, 90%).

In large-scale preparations most of the acetone used for the reaction could be recovered by distillation of the reaction mixture under reduced pressure and was suitable for recycling.

Preparation of 41

$PhCH(OMe)_2$ (2.25 mL, 15 mol equiv) was added to methyl α-D-glucoside (**15**, 194 mg, 1 mmol) followed by the addition of $In(OTf)_3$ (4 mg/100 mg sugar derivative) and the reaction mixture was stirred until dissolution of the sugar derivative occurred (cf. 2 min). TLC (EtOAc:*n*-Hex, 2:1, v/v) at this stage showed completion of the reaction. Aqueous workup followed by column chromatography (eluent, EtOAc:*n*-Hex, 1:4 followed by 1:1, v/v) yielded crystalline **41** (235 mg, 83%).

General Procedure for the Hydrolysis of Acetals

To the respective sugar derivative dissolved in aq dioxane (10%, v/v) was added $In(OTf)_3$, and the solution was stirred at 50°C to 70°C until TLC showed complete conversion. The reaction mixture was then concentrated under reduced pressure and either directly passed through a column of silica gel for purification (eluent, 25% MeOH in CH_2Cl_2) or subjected to acetylation as described above to yield the corresponding acetylated sugar derivative.

The following compounds were prepared:

Compounds **46**,[41] **15** (from **47**[42]), **49**[44] (from **48**[44]), **51**[46](from**50**[45]), and **53**[17] (from **52**[43]).

Preparation of 46/5

To a solution of diacetone glucose (**21**, 100 mg) in aq dioxane (1 mL, 10%, v/v) was added $In(OTf)_3$ (10 mg) and it was stirred at 50°C for 2 h when TLC (EtOAc) showed completion of the reaction. It was then concentrated to a small

volume and the product was isolated by passing through a short column of silica gel (eluent, EtOAc:*n*-Hex, 2:1) to yield the desired mono-*O*-acetone glucose **46** as white solid (60 mg, 71%). Similar reaction carried out at 70°C for 1 h yielded **46** in an isolated yield of 75% (64 mg) and at 50°C for 10 h yielded D-glucose (**5**, 59 mg) in 85% isolated yield.

General Procedure for Thioglycosylation

To a solution of the respective per-*O*-acetylated sugar derivative in CH_2Cl_2 (or DCE) was added benzyl mercaptan (3 mol equiv) followed by $In(OTf)_3$ (0.25 mol equiv), and the solution was stirred at 40°C (50°C could be used if DCE is employed as solvent, which was found to result in faster reactions) until TLC showed complete consumption of the starting material. Aqueous workup followed by purification by crystallization (Et_2O-*n*-Hex) yielded the desired thioglycoside.

Compound prepared in this manner: **56**[17] from **55**.[16]

Preparation of 56

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranose (**55**, 238 mg, 0.5 mmol) was taken up in CH_2Cl_2 (2 mL) and to this was added benzyl mercaptan (85 μL, 0.55 mmol) followed by $In(OTf)_3$ (140 mg, 0.25 mmol). It was then stirred for 2 h at 40°C when TLC (EtOAc:*n*-Hex, 1:4) showed completion of the reaction. The mixture was then diluted with CH_2Cl_2 and was subjected to aq workup following which the product (**56**) was obtained as crystalline solid (260 mg, 96%).

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