# Triphenylphosphine Polymer-Bound/Iodine Complex: A Suitable Reagent for the Preparation of *O*-Isopropylidene Sugar Derivatives

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**Abstract:** *O*-Isopropylidene derivatives of sugars are readily prepared by using the Lewis acid and dehydrating agent triphenylphosphine polymer-bound/$I_2$ complex. This new method is characterized by smooth, non-equilibrating reaction conditions and a very clean, simple work-up, making it particularly suitable for O-isopropylidenation of sugars under mild conditions and with low environmental impact.

**Key words:** acetals, carbohydrates, triarylphosphine–iodine complex, *O*-isopropylidene, acetonation

The condensation of acetone with aldoses and ketoses leading to the formation of isopropylidene derivatives has been widely used in synthesis to protect hydroxyl functions in carbohydrate chemistry. Furthermore, *O*-isopropylidene derivatives, for instance 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose derivatives, have shown anti-inflammatory and antipyretic activities as well as a very low toxicity.[1]

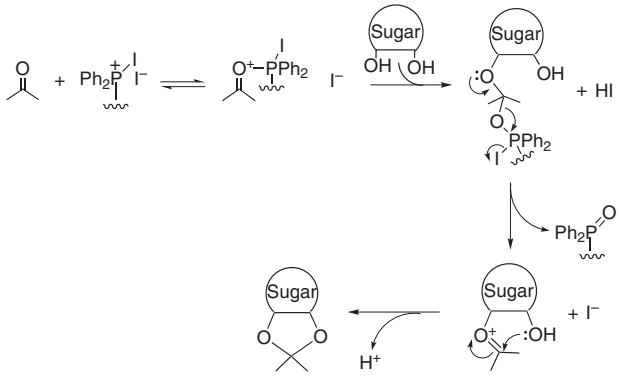
The conventional method for the preparation of such derivatives consists in the condensation of a vicinal diol with acetone, in the presence of an acidic catalyst, under anhydrous conditions. Many different agents have been used as catalysts, including mineral acids,[2] anhydrous zinc chloride together with phosphoric acid,[3] ion exchange resins,[4] anhydrous copper(II) sulfate,[5] iodine,[6] anhydrous ferric chloride,[7] $BF_3{\cdot}OEt_2$,[8] anhydrous $AlCl_3$[9] and, more recently, zeolites.[10]

Under the equilibrating conditions, water is formed which must be removed from the reaction mixture using either physical or chemical methods.[11] Generally, the major products obtained from these reactions are those which are thermodynamically favored. Otherwise, kinetic control can be obtained using other reagents for condensation, namely 2-methoxypropene in the presence of *p*-toluenesulfonic acid.[12]

We wish to report a new method based on the use of a triphenylphosphine polymer-bound/iodine complex for the thermodynamic acetonation of sugars in high yields, in anhydrous medium, avoiding water formation. Recent interest in the development of environmentally benign synthesis has led to a renewed interest in developing polymer-bound metal catalysts and reagents for organic synthesis that maintain high activity.[13] The reagents bound on polymeric supports offer a number of advantages over traditional solution-phase chemistry.

The triphenylphosphine polymer-bound/halogen complex is a Lewis acid and a dehydrating agent widely used in miscellaneous reactions[14] with low environmental impact. In fact, it avoids contamination from by-products and use of solvents, which are not environmentally friendly, in the purification processes. Triphenylphosphine polymer-bound/iodine complex is an easy to prepare,[15] handy, semi-crystalline solid, reasonably stable at room temperature. When dried and kept properly, it can be stored for weeks at room temperature, under $N_2$ atmosphere. The somewhat high cost of the starting triphenylphosphine polymer-bound does not actually represent a limitation of this procedure, if one considers that the polymer-linked phosphine oxide generally obtained from the reaction can be readily filtered off and reduced to the original phosphine form with trichlorosilane.[16]

Under our conditions, the sugar is added to a suspension of triphenyl phosphine polymer-bound/iodine complex (polystyryl diphenyl iodophosphonium iodide) in anhydrous acetone.[17] An adduct is first formed, due to the presence of the positively charged phosphorous atom in the complex and the electron-rich carbonyl oxygen of acetone, which exposes the carbonyl carbon atom to undergo nucleophilic attack by a first hydroxyl group of the sugar molecule (Scheme 1). The subsequent non-equilibrium step of the reaction is the loss of polymer-linked phosphine oxide and thereby formation of an oxygen-stabilized carbocation, known to be intermediate in the acetalization reaction.




**Scheme 1**

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This latter can undergo the intramolecular attack by a second hydroxyl group present in the sugar molecule to afford the final *O*-isopropylidene derivative. The reaction is carried out under mild conditions, at room temperature, and is generally fast and high-yielding affording the thermodynamically more stable isopropylidene derivatives. Results obtained from the acetonation of miscellaneous sugars, such as L-arabinose, D-fructose, D- and L-galactose, D-glucose, D-mannose, D-ribose, L-sorbose, D-glucitol, using a triphenyl phosphine polymer-bound/iodine complex/sugar ratio of 2:1 are shown in Table 1. Each acetonation has been compared with the best one reported in literature.[2,3,6,7,18–23]

1,2:3,4-Di-*O*-isopropylidene-D-ribopyranose is a known compound[2b] that usually accompanies 2,3-*O*-isopropylidene-D-ribofuranose when the latter is prepared from D-ribose. However, to the best of our knowledge no intentional preparations, and consequently yields are reported for it in literature.

On the other hand, under our conditions using only one equivalent of triphenylphosphine polymer-bound/iodine complex D-ribose affords the pure mono-*O*-isopropylidene derivative, as well as, the sole di-*O*-isopropylidene derivative when treated with two equivalents.

All the acetonides reported in Table 1 were obtained within 30 minutes by simple filtration of polymer bound phosphine oxide, the only by-product of the reaction, with high purity. All the physical data reported in Table 1 within parentheses were withdrawn from the literature. A comparison of the data shows that the yields of thermodinamically more stable isopropylidene derivatives are often higher than those of other methods.

**Table 1** *O*-Isopropylidene Derivatives of Miscellaneous Sugars[a]

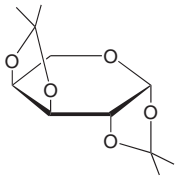
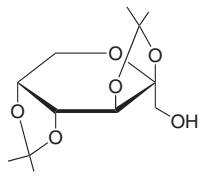
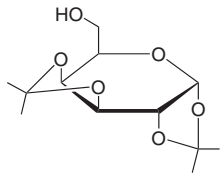
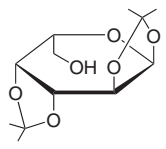
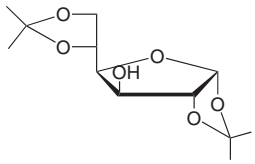
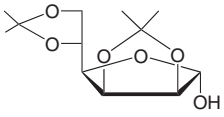
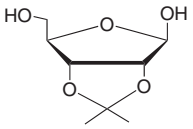
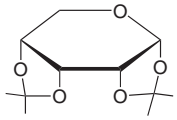
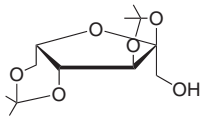
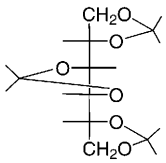
| Isopropylidene derivatives from | Yield(%) | Mp (°C) | $[\alpha]_D^{25}$ | $^1$H NMR ($CDCl_3$) Elemental Analysis |
|---|---|---|---|---|
|  L-Arabinose | 95 (85)[6] | 40–41 (40–41)[18] | +6.1 (*c* = 1.5, $H_2O$) +5.8 (*c* = *unknown*, $H_2O$)[7] | 1.32 (s, 3 H, $CH_3$), 1.41 (s, 3 H, $CH_3$), 1.47 (s, 3 H, $CH_3$), 1.52 (s, 3 H, $CH_3$), 3.64 (d, $J_{5a,5b}$ = 12.5 Hz, 1 H, $H_a$-5), 3.82 (d, $J_{5b,5a}$ = 12.5 Hz, 1 H, $H_b$-5), 4.23 (br d, $J_{4,3}$ = 7.5 Hz, 1 H, H-4), 4.30 (dd, $J_{2,1}$ = 5.3 Hz, $J_{2,3}$ = 2.3 Hz, 1 H, H-2), 4.54 (dd, $J_{3,4}$ = 7.5 Hz, $J_{3,2}$ = 2.3 Hz, 1 H, H-3), 5.48 (d, $J_{1,2}$ = 5.3 Hz, 1 H, H-1). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.47; H, 7.90. |
|  D-Fructose | 90 (55)[19] | 95–96 (97)[19] | –32.9 (*c* = 1.5, $H_2O$) –24.7 (*c* = 1.1, $CHCl_3$)[19] | 1.28 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$), 1.35 (s, 3 H, $CH_3$), 1.38 (s, 3 H, $CH_3$), 2.28 (br s, 1 H, OH), 3.62 (d, $J_{1a,1b}$ = 10.7 Hz, 1 H, $H_a$-1), 3.66 (d, $J_{1b,1a}$ = 10.7 Hz, 1 H, $H_b$-1), 3.79 (dd, $J_{6a,6b}$ = 13.0 Hz, $J_{6a,5}$ = 0.8 Hz, 1 H, $H_a$-6), 3.88 (dd, $J_{6b,6a}$ = 13.0 Hz, $J_{6b,5}$ = 2.0 Hz, 1 H, $H_b$-6), 4.21 (ddd, $J_{5,4}$ = 7.7 Hz, $J_{5,6b}$ = 2.0 Hz, $J_{5,6a}$ = 0.8 Hz, 1 H, H-5), 4.32 (dd, $J_{3,4}$ = 2.9 Hz, 1 H, H-3), 4.57 (dd, $J_{4,5}$ = 7.7 Hz, $J_{4,3}$ = 2.9 Hz, 1 H, H-4). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.45; H, 7.69. |
|  D-Galactose | 95 (76–92)[3] | Oil (oil)[3] | –59.5 (*c* = 1.5, $CHCl_3$) –55.0 (*c* = 3.6, $CHCl_3$)[3] | 1.32 (s, 6 H, $CH_3$), 1.44 (s, 3 H, $CH_3$), 1.55 (s, 3 H, $CH_3$), 3.62–3.81 (m, 1 H, $H_a$-6), 3.84–3.95 (m, 2 H, $H_b$-6, H-5), 4.28 (dd, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 1.5 Hz 1 H, H-4), 4.34 (dd, $J_{2,1}$ = 5.0 Hz, $J_{2,3}$ = 2.0 Hz, 1 H, H-2), 4.62 (dd, $J_{3,4}$ = 8.1 Hz, $J_{3,2}$ = 2.0 Hz, 1 H, H-3), 5.57 (d, $J_{1,2}$ = 5.0 Hz, 1 H, H-1) Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.29; H, 7.71. |
|  L-Galactose | 97 (58)[20] | Syrup (syrup)[20] | +57.0 (*c* = 0.9, $CHCl_3$) *(not reported)* | Superimposable to that of the D-enantiomer Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.48; H, 7.76. |

**Table 1** *O*-Isopropylidene Derivatives of Miscellaneous Sugars[a] (continued)

| Isopropylidene derivatives from | Yield(%) | Mp (°C) | $[\alpha]_D^{25}$ | $^1$H NMR ($CDCl_3$) Elemental Analysis |
|---|---|---|---|---|
|  D-Glucose | 95 (91)[3] | 108–109 (110–111)[3] | –18.5 (*c* = 5.0, $H_2O$) –18.5 (*c* = 5.0, $H_2O$)[3] | 1.30 (s, 3 H, $CH_3$), 1.35 (s, 3 H, $CH_3$), 1.43 (s, 3 H, $CH_3$), 1.48 (s, 3 H, $CH_3$), 3.97 (dd, $J_{6a,6b}$ = 8.7 Hz, $J_{6a,5}$ = 5.1 Hz, 1 H, $H_a$-6), 4.04 (dd, $J_{4,5}$ = 8.0 Hz, $J_{4,3}$ = 2.9 Hz, 1 H, H-4), 4.15 (dd, $J_{6b,6a}$ = 8.7 Hz, $J_{6b,5}$ = 6.6 Hz, 1 H, $H_b$-6), 4.25–4.38 (m, 2 H, H-3, H-5), 4.51 (d, $J_{2,1}$ = 3.7 Hz, 1 H, H-2), 5.92 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.43; H, 7.72. |
|  D-Mannose | 95 (92)[3] | 121–122 (122–123)[3] | +16.6 (*c* = 2.5, EtOH) +16.0 (*c* = 2.6, EtOH)[3] | 1.32 (s, 3 H, $CH_3$), 1.38 (s, 3 H, $CH_3$), 1.46 (s, 3 H, $CH_3$), 1.48 (s, 3 H, $CH_3$), 4.03 (dd, $J_{6a,6b}$ = 10.2 Hz, $J_{6a,5}$ = 6.1 Hz, 1 H, $H_a$-6), 4.08 (dd, $J_{6b,6a}$ = 10.2 Hz, $J_{6b,5}$ = 6.8 Hz, 1 H, $H_b$-6), 4.20 (dd, $J_{4,3}$ = 7.2 Hz, $J_{4,5}$ = 3.7 Hz, 1 H, H-4), 4.38–4.44 (m, 1 H, H-5), 4.63 (d, $J_{2,3}$ = 6.2 Hz, 1 H, H-2), 4.81 (dd, $J_{3,4}$ = 7.2 Hz, $J_{3,2}$ = 6.2 Hz, 1 H, H-3), 5.39 (s, 1 H, H-1). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.30; H, 7.73. |
|  D-Ribose | 95 (90–93)[21a,b] | Oil (oil)[21c] | –24.7 (*c* = 1.1, $CHCl_3$) –25.9 (*c* = 1.1, $CHCl_3$)[21c] | 1.32 (s, 3 H, $CH_3$), 1.48 (s, 3 H, $CH_3$), 3.55–3.83 (m, 2 H, H-5), 4.40 (br s, 1 H, H-4), 4.57 (d, $J_{2,3}$ = 6.0 Hz, 1 H, H-2), 4.85 (d, $J_{3,2}$ = 6.0 Hz, 1 H, H-3), 5.42 (s, 1 H, H-1). Anal. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.41; H, 7.39. |
|  D-Ribose | 92 (as by-product) [2b] | 70–71 (68–69)[2b] | –55.0 (*c* = 1.1, $CHCl_3$) –51.0 (*c* = 0.6, $CHCl_3$)[2b] | 1.33 (s, 3 H, $CH_3$), 1.37 (s, 3 H, $CH_3$), 1.55 (s, 3 H, $CH_3$), 1.62 (s, 3 H, $CH_3$), 3.83 (dd, $J_{5a,5b}$ = 12.1 Hz, $J_{5a,4}$ = 9.7 Hz, 1 H, $H_a$-5), 4.01 (dd, $J_{5b,5a}$ = 12.1 Hz, $J_{5b,4}$ = 7.7 Hz, 1 H, $H_b$-5), 4.24 (dd, $J_{2,3}$ = 7.9 Hz, $J_{2,1}$ = 5.2 Hz, 1 H, H-2), 4.40–4.53 (m, 2 H, H-3, H-4), 5.43 (d, $J_{1,2}$ = 5.2 Hz, 1 H, H-1). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.50; H, 7.88. |
|  L-Sorbose | 95 (96–99)[22] | 80–81 (77–78)[22] | –14.3 (*c* = 1.5, $Me_2CO$) –18.1 (*c* = 1.5, $Me_2CO$)[22] | 1.37 (s, 6 H, $CH_3$), 1.44 (s, 3 H, $CH_3$), 1.51 (s, 3 H, $CH_3$), 2.31 (t, $J_{OH,1}$ = 7.5 Hz, 1 H, OH), 3.78 (dd, $J_{1a,1b}$ = 12.5 Hz, $J_{1a,OH}$ = 7.5 Hz, 1 H, $H_a$-1), 3.87 (dd, $J_{1b,1a}$ = 12.5 Hz, $J_{1b,OH}$ = 7.5 Hz, 1 H, $H_b$-1), 3.92–4.92 (m, 3 H, H-6, H-5),4.32 (d, $J_{4,3}$ = 1.6 Hz, 1 H, H-4), 4.48 ($J_{4,3}$ = 1.6 Hz, 1 H, H-3). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.29; H, 7.76. |
|  D-Glucitol | 97 (53)[23] | 45–46 (45–46)[23] | +12.7 (*c* = 1.1; EtOH) +14.2 (*c* = *unknown*; EtOH)[23] | 1.37 (s, 3 H, $CH_3$), 1.38 (s, 3 H, $CH_3$), 1.42 (s, 12 H, 4 × $CH_3$), 3.69–4.12 (m, 8 H, H-1, H-2, H-3, H-4, H-5, H-6). Anal. Calcd for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67. Found: C, 59.48; H, 8.69. |

[a] Literature data within parentheses.

$^1$H NMR spectra were taken on Bruker DRX-400 and Varian Gemini 200 spectrometers. Optical rotations were measured on a Jasco P-1010 instrument (1.0 dm cell). Combustion analyses were performed on Perkin-Elmer Series II 2400, CHNS analyzer. TLC analyses were carried out on silica gel Merck 60 F254 plates (0.2 mm layer thickness). Column chromatography was performed on Merck Kieselgel 60 (70–230 mesh). Anhyd acetone was distilled immediately before use. Triphenyl phosphine polymer-bound was purchased from Fluka Chemical Co.

**Preparation of 1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose; Typical Procedure**

To a magnetically stirred suspension of anhyd polystyryl diphenyl phosphine (1.12 g, ca. 3.34 phosphine units) in anhyd acetone (10 mL) at r.t., a solution of $I_2$ (0.85 g, 3.34 mmol) in the same solvent (30 mL) was added dropwise in the dark and under dry $N_2$ atmosphere. After 15 min, solid D-glucopyranose (0.33 g, 1.67 mmol) was added in one portion to the suspension. TLC monitoring ($CHCl_3$–MeOH, 9:1) showed that the starting sugar was completely consumed within 30 min. The reaction mixture was then filtered

through a glass sinter funnel and washed with acetone. The solvent was removed under reduced pressure and the solid residue was recrystallized from $CHCl_3$–hexane (1:2) to give the final product (0.41 g, 95% yield).

Under the same conditions, the *O*-isopropylidene derivatives shown in Table 1 were prepared using one equivalent of triphenyl phosphine polymer-bound/iodine complex per acetonide group expected in the product.

## Acknowledgment

$^1$H NMR spectra were performed at Centro Interdipartimentale di Metodologie Chimico-Fisiche, Università di Napoli Federico II.

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