REPLACEMENT OF SECONDARY HYDROXYL IN 2,3,6-TRI-O-BENZOYL-α-METHYL-D-GALACTOPYRANOSIDE BY HALOGEN AND THIOCYANATE USING TRIVALENT PHOSPHORUS DERIVATIVES

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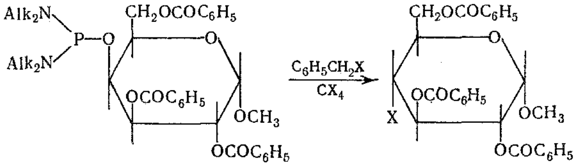
Considerable difficulties are encountered in replacing the secondary hydroxyl in monosaccharides by other functional groups. In view of this it seemed of interest to use the substitutive dephosphorylation reaction, previously described by us [1], for this purpose.

The alkylation of the methyl-4-tetraalkyldiamidophosphite of 2,3,6-tri-O-benzoylgalacto-α-D-pyranoside (I) with either $C_6H_5CH_2Br$ of CCl_4 gives the corresponding 4-bromo- and 4-chlorodesoxy derivatives.



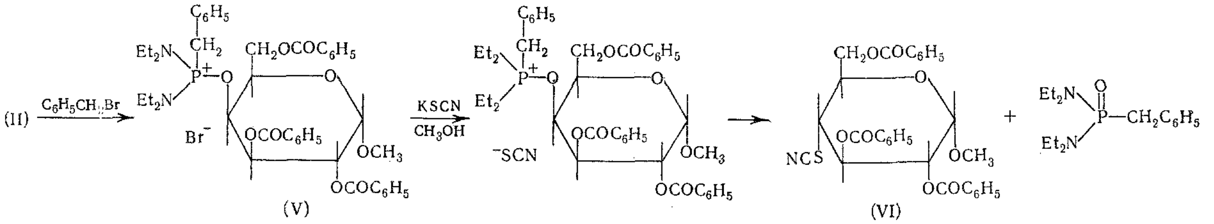
(I), (II) (III), (IV)

Alk = CH_3 (I), Alk = C_2H_5 (II), X = Br (III), Cl (IV)

The structure of the obtained products is confirmed by the fact that, after removal of the protective groups and reduction over Raney Ni, 4-desoxy-D-xylohexose is formed, which, based on the paper chromatography data, is identical with the authentic specimen.

The picture in the NMR spectrum for the splitting of the proton at C_4 proved to be complicated, and did not lend itself to unambiguous treatment, but the presence of a triplet with a spin–spin coupling constant of 10 Hz for the C_3 proton testifies to the fact that the obtained compounds have the gluco configuration.

The reaction of $C_6H_5CH_2Br$ with tetraethyldiamidophosphite (II) gives the quasiphosphonium salt, which is stable at room temperature. Its treatment with alcoholic KSCN solution makes it possible to obtain a new salt, which when heated undergoes substitutive dephosphorylation with the formation of the thiocyano derivative (VI)



(V) (VI)

The IR spectrum of the obtained compound contains a band at 2150 cm^{-1}, which is characteristic for alkyl thiocyanates. The compound has the gluco configuration, since in its properties it corresponds completely to the authentic specimen, which was obtained by counter synthesis.

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EXPERIMENTAL METHOD

The experiments with the trivalent phosphorus derivatives were run in a dry argon atmosphere. The TLC and column chromatography were run on Al_2O_3 and on SiO_2 (II activity) in chloroform.

To detect the compounds we used either I_2 vapors or H_2SO_4, with subsequent heating.

4-Tetramethyldiamidophosphite of 2,3,6-Tri-O-benzoyl-α-methyl-D-galactopyranoside (I). A mixture of 4.65 g of methyl-2,3,6-tri-O-benzoyl-α-D-galactopyranoside [2] and 4.8 g of hexaethyltriamidophosphite was heated for 5 h at 110-120°C using a water-jet pump (200-100 mm). We obtained 5.8 g of (I) as a viscous yellowish sirup. The crude product was used in the substitutive dephosphorylation reactions.

4-Tetraethyldiamidophosphite of 2,3,6-Tri-O-benzoyl-α-methyl-D-galactopyranoside (II). In a similar manner, from 2.5 g of methyl-2,3,6-tri-O-benzoyl-α-D-galactopyranoside and 3.6 g of hexaethyltriamidophosphite at 110-120° was obtained 3.3 g of (II); it decomposes during TLC. The product was used without purification in the subsequent transformations.

4-Bromo-4-desoxy-2,3,6-O-benzoyl-α-methyl-D-galactopyranoside (IV). A mixture of 3.1 g of (I) and 3.4 g of $C_6H_5CH_2Br$ was heated at 120° for 6 h. The excess $C_6H_5CH_2Br$ was distilled off and the residue was chromatographed on an SiO_2 column. We obtained 4.4 g (78%) of (III), $[\alpha]_D^{20}$ + 59° (C 0.1, chloroform). Found: C 58.88; H 4.22; Br. 14.11%. $C_{28}H_{25}O_8Br$. Calculated: C 59.05; H 4.39; Br 14.05%.

4-Chloro-4-desoxy-2,3,6-O-benzoyl-α-methyl-D-galactopyranoside (IV). In a similar manner, from 3.12 g of (I) and 1.54 g of CCl_4 in 50 ml of DMF, at 120° for 5 h, was obtained 3.8 g (74%) of (IV) as a colorless sirup, $[\alpha]_D^{20}$ + 61.5° (C 0.1, chloroform). Found: C 64.13; H 4.74; Cl 6.66%. $C_{28}H_{25}O_8Cl$. Calculated: C 64.08; H 4.76; Cl 6.76%.

2,3,6-O-Benzoyl-α-methyl-D-galactopyranoside 4-Tetraethyldiamidophosphite Bromobenzylate (V). To 3.4 g of (II) in 15 ml of absolute ether was added 0.9 g of $C_6H_5CH_2Br$, after which the mixture was allowed to stand for 2-3 h at 20° and then evaporated in vacuo. We obtained 4.3 g of (V), mp 111°. Found: C 60.30; H 6.11; N 3.27; P 3.59%. $C_{43}H_{51}N_2O_9P$. Calculated: C 60.56; H 6.10; N 3.26; P 3.63%.

4-Thiocyano-4-desoxy-2,3,6-O-benzoyl-α-methyl-D-galactopyranoside (III). To 2.2 g of (V) in 10 ml of methanol was added 1 g of KSCN in 10 ml of methanol. The mixture was filtered, the methanol was distilled off, and the residue was heated in 10 ml of DMF at 120° for 2 h. After this the mixture was filtered and evaporated using the vacuum of an oil pump. We obtained 2.1 g of residue as a brownish sirup. The product was chromatographed on an Al_2O_3 column. We obtained 0.87 g (65%) of (III), mp 189-191°, $[\alpha]_D^{20}$ + 65° (C 0.1, chloroform); cf. [3]. Found: C 63.61; H 4.54; N 2.39%. $C_{29}H_{25}O_8NS$. Calculated: C 63.61; H 4.57; N 2.55%.

CONCLUSIONS

1. Some secondary halodesoxysaccharides were synthesized on the basis of the substitutive dephosphorylation method.

2. A new route was proposed for replacing a secondary hydroxyl in carbohydrates by the thiocyano group employing trivalent phosphorus derivatives.

LITERATURE CITED

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