The transphosphorylation of β-cyclodextrin perphosphites: a new supramolecular property

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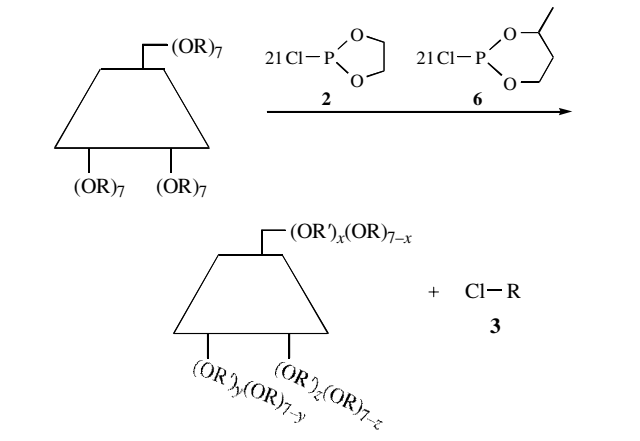
10.1070/MC2001v011n06ABEH001487

β-Cyclodextrin perphosphite **1**, R = 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl, exhibits an unusual transphosphorylation reaction with chlorophosphites; the inclusion of adamantane into the cyclodextrin cavity substantially inhibits this reaction.

Cyclodextrins are of interest to organic chemistry because of their great potential in synthetic applications,[1] as well the possibility of designing novel supramolecular architectures exploiting the intramolecular chiral hydrophobic cavities of these compounds.[2] However, the role played by the cyclodextrin cavity in binding and chemical transformations is not clearly understood. In particular, such considerations have played little part in the analysis of the transformation of organophosphorus compounds in contact with cyclodextrins. In this context, we examined the chemical properties of β-cyclodextrin perphosphite **1**, R = 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl, and found that it has a tendency to undergo transphosphorylation during its interaction with chlorophosphites.[3] Note that such a reaction was previously unknown: the phosphites of carbohydrates and related compounds do not enter into such reactions. Thus, the transphosphorylation of β-cyclodextrin perphosphites is an unique phenomenon and, therefore, we aimed to investigate its chemical nature. We assumed that a transphosphorylating reagent could be included in the cyclodextrin cavity and then transformed at a supramolecular level. This transformation consists in bringing together the covalently bound phosphite groups of host and guest molecules followed by the redistribution of the bonds to form new perphosphites of β-cyclodextrin. The resulting β-cyclodextrin products have more compact substituents and hence are more stable compounds. To test this hypothesis on the mechanism of transphosphorylation, we performed transphosphorylation in the presence of adamantane. It is well known that the structure and size of an adamantane molecule fit to the structure and size of the cavity of β-cyclodextrin (and many its derivatives); therefore, β-cyclodextrins readily form stable inclusion compounds with adamantane.[4] Evidently, analogous adamantane inclusion compounds from β-cyclodextrin perphosphites **1** would not permit the inclusion of a transphosphorylating agent. Since this experiment showed that adamantane 'turned off' the transphosphorylation reaction, the hypothesis on the supramolecular aspects of the original transphosphorylation reaction was confirmed experimentally.

The course of the transformation was quantitatively monitored by ^{31}P NMR spectroscopy. The integration of appropriate signals showed the accumulation of chlorophosphite **3** (147 ppm) and the redistribution of the initial signals of the phosphorus-containing residues in initial compound **1** (121 ppm) and product **4** (121 and 135 ppm). We found that, in the absence of adamantane, the reaction proceeded by 60% at 20 °C after 2 h and by 80% at 60 °C after 1 h (although no further reaction then occured).† Under the same conditions in the presence of 2 equiv. of adamantane, the reaction proceeded by only 5% and even after heating at 80 °C for 72 h the transphosphorylation proceeded by only 20%.‡

In a separate experiment, we found that the transphosphorylation of β-cyclodextrin perphosphite **1**, R = 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl, also occurs with other chlorocyclophosphites, namely, 2-chloro-4,5-dimethyl-1,3,2-dioxaphospholane **5**, 2-chloro-4-methyl-1,3,2-dioxaphosphorinane **6** and 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane. In these cases, the extent of reaction was 60, 50 or 40%, respectively (at 60 °C for 1 h).

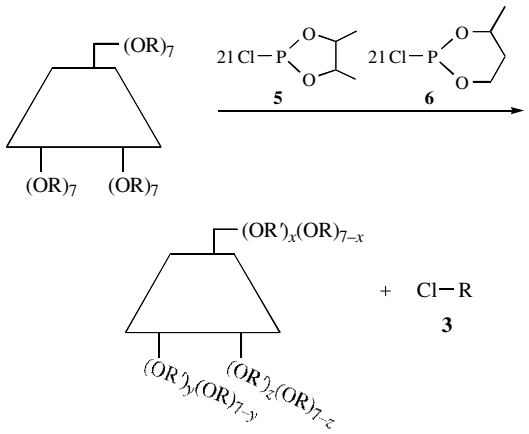


Unexpected results were obtained in the transphosphorylation with an equimolecular mixture of two chlorophosphites **2** and **6** (1:1).§ In this case, the reaction slows down sharply: according

† Chlorophosphite **2** (0.27 g, 2.1 mmol) was added to a solution of perphosphite **1** (0.39 g, 0.1 mmol) in 10 ml of benzene at 25 °C with stirring. The ^{31}P NMR spectrum of the reaction mixture (25 °C, 2 h) δ: 168 (**2**) and 147 (**3**), 134, 122 (**4**) in an integral ratio of 2:3:3:2; (60 °C, 1 h) δ: 168 (**2**) and 147 (**3**), 134, 122 (**4**) in an integral ratio of 1:4:4:1.

‡ Chlorophosphite **2** (0.27 g, 2.1 mmol) was added to a solution of perphosphite **1** (0.39 g, 0.1 mmol) and adamantane (0.027 g, 0.2 mmol) in 10 ml of benzene at 25 °C with stirring. The ^{31}P NMR spectrum of the reaction mixture (25 °C, 2 h) δ: 168 (**2**) and 147 (**3**), 134, 122 (**4**) in an integral ratio of 19:1:1:19; (60 °C, 1 h) δ: 168 (**2**) and 147 (**3**), 134, 122 (**4**) in an integral ratio of 4:1:1:4.

§ Chlorophosphites **2** and **6** (2.1 mmol of each) were added to a solution of perphosphite **1** (0.39 g, 0.1 mmol) in 10 ml of benzene at 25 °C with stirring.



to ^{31}P NMR data, the signal of chlorophosphite **3** appears only after heating at 80 °C for 24 h. We presume that this phenomenon is due to competition between chlorophosphites **2** and **6** at both steps (*a* and *b*) needed for the transphosphorylation: namely, the inclusion into a cyclodextrin cavity (*a*) and the interaction with neopentylenephosphite residues (*b*). This supposition is confirmed by the fact that the use of the same conditions with an equimolecular mixture of two chlorophosphites **5** and **6** does not inhibit the reaction (50% substitution after 2 h at 60 °C).¶ This can be explained by an increased affinity of chlorophosphite **5**, in comparison with **2**, for the cyclodextrin cavity. Here, the difference in the strength of the inclusion compounds from the former and latter reagents is not as great, and the reaction proceeds normally.

Therefore, we can conclude that the discovered transphosphorylation of per-P^{III}-containing cyclodextrins **1**, R = 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-yl is, probably, a result of complex supramolecular interactions between cyclodextrin derivatives and chlorophosphites.

References

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Received: 18th June 2001; Com. 01/1813

¶ Chlorophosphites **5** and **6** (2.1 mmol of each) were added to a solution of perphosphite **1** (0.39 g, 0.1 mmol) in 10 ml of benzene at 25 °C with stirring.