The side-chain CD obtained indicates that a positive intense CD band at 230 nm, whose pair is an ~217-nm negative band, originates from the formation of excitation coupling between indole chromophores. Moreover, the greatly different intensities of these two excitation bands and the existence of an ~207-nm positive band show that the ρμ1−μ2 mechanism may not only occur between 1Bb transitions but between 1Bb and 1Bα transitions.

A more detailed investigation for optical activity of PLT is now in progress by our group.

Our FDCD technique for PLT can be applied to the conformational analysis of similar peptides such as poly-L-tyrosine.

Acknowledgment. We thank Dr. Tsugikazu Tomono and Tohru Suzuki (Department of Research and Development, Japanese Red Cross Plasma Fractionation Center) for permission to use the J-500C spectropolarimeter. We also thank Yasunobu Komiyama for the contribution to the early development of our FDCD instrument.

Thioxanthones as High Turnover Catalytic Templates in Directed Chlorination Reactions

Ronald Breslow and Monica P. Mehta

Department of Chemistry, Columbia University
New York, New York 10027

Received June 13, 1986

We have recently reported\(^7\) that the steroid nicotinate ester 1 is catalytically chlorinated at C-9 by forming a mixed complex with Ni\(^{2+}\) or Cu\(^{2+}\) and template 2. Then PhICI\(_2\) with irradiation, starts a chain process in which a chlorine atom is first transferred to the template and then attacks the steroid hydrogen, in a radical relay\(^2\) mechanism. Remarkably, under appropriate conditions the catalyst 2 undergoes \(10^8\) turnovers.

The side-chain CD obtained indicates a positive intense CD band at 230 nm, whose pair is an ~217-nm negative band, originates from the formation of excitation coupling between indole chromophores. Moreover, the greatly different intensities of these two excitation bands and the existence of an ~207-nm positive band show that the ρμ1−μ2 mechanism may not only occur between 1Bb transitions but between 1Bb and 1Bα transitions.

A more detailed investigation for optical activity of PLT is now in progress by our group.

Our FDCD technique for PLT can be applied to the conformational analysis of similar peptides such as poly-L-tyrosine.

Acknowledgment. We thank Dr. Tsugikazu Tomono and Tohru Suzuki (Department of Research and Development, Japanese Red Cross Plasma Fractionation Center) for permission to use the J-500C spectropolarimeter. We also thank Yasunobu Komiyama for the contribution to the early development of our FDCD instrument.

### Thioxanthones as High Turnover Catalytic Templates in Directed Chlorination Reactions

Ronald Breslow* and Monica P. Mehta

Department of Chemistry, Columbia University
New York, New York 10027

We have recently reported\(^\text{1}1\) that the steroid nicotinate ester 2 is catalytically chlorinated at C-9 by forming a mixed complex with Ni\(^{2+}\) or Cu\(^{2+}\) and template 2. Then PhICI\(_2\), with irradiation, starts a chain process in which a chlorine atom is first transferred to the template and then attacks the steroid hydrogen, in a radical relay\(^2\) mechanism. Remarkably, under appropriate conditions the catalyst 2 undergoes \(10^8\) turnovers.

---


Not all catalytic reactions with 2 show such high turnovers. Chlorination of 3 at C-9, or of 4 at C-9, were successful with NiII and 2 because of metal coordination to the OH but required stoichiometric amounts.1 We have now devised a new template catalyst that indeed performs the important C-9 chlorination of 3 with reasonable turnovers. At the same time, we have developed evidence, described in the accompanying paper, that the remarkably high turnovers sometimes observed with 2 and with the new template result from a special new bifunctional chlorination mechanism.

Since the eventual decomposition of 2 involves replacement of iodine by chlorine,1 we examined the use of sulfur atom templates that might be more stable. The diphenyl sulfide analogue 5 was too easily oxidized, and even a related thiophene system 6 showed only 10^2 turnovers with 1. However, the thioxanthone template 7 was an excellent catalyst. Substrate 1 was 80% converted to C-9 chloroestoroid, with 20% recovered 1, when 15 mM 1 was irradiated with 3 equiv. of PhICl2 and 5 equiv. of undissolved KOAc in CH2Cl2 with 15 \times 10^{-5} M NiII and 15 \times 10^{-12} M 7 for 10 min (275-W sunlamp) at 0 °C (or at 20 °C) and then allowed to react further without irradiation for 1.5 h. Thus 10^3 to 10^12 turnovers of 7 are occurring. Template 7 also catalyzed the C-9 chlorination of 3 and 4, with ca. 10^2 turnovers.

Indeed, reaction of the decane-1,10-diol derivative 9a at 15 mM with 3 equiv of PhICl2 and 5 equiv of KOAc along with 15 \times 10^{-4} M 8 and 30 \times 10^{-3} M NiII (ClO4)_2 under irradiation for 1 h at 0 °C afforded the monochlorinated 9a with 32% recovered 9a (at 15 \times 10^{-3} M 8, no 9a is detected). By methods we have described earlier4 we were able to establish that the chlorination occurs essentially exclusively at the middle carbon C-5, as expected if 9a coordinates to a fully extended conformation of the 8-[NiII]-2 complex. This conformation is apparently the preferred one, because of electrostatic repulsion by the NiII ions, since the shorter hexanediol and butanediol derivatives 9b and 9c are not chlorinated by the 8-[NiII]-2 complex. Models show that they should also be able to bind at both ends and be chlorinated, if the template does not have the fully extended conformation.

This work shows that catalytic templates based on the thioxanthone system can have even better turnover numbers with steroids, compared with aryl iodide templates. Even a simple underivatized steroid such as 3 can be catalytically functionalized. The thioxanthone system also easily carries more than one binding group, as in 8, to permit selective catalytic reactions on flexible substrates. In the accompanying paper10 we will describe the evidence that some thioxanthone or aryl iodide catalysts involve a novel bifunctional mechanism.

Acknowledgment. This work has been supported by the NSF.

A Novel Bifunctional Chlorination Mechanism in Template Catalyzed Directed Functionalization with High Effective Molarities and Rates Approaching Diffusion Control

Ronald Breslow* and Monica P. Mehta

Department of Chemistry, Columbia University
New York, New York 10027
Received June 13, 1986

We have described the catalytic chlorination of 3α-cholestanoyl nicoatinate (1) by mixed-metal complexes with an aryl iodide template (2) and a thioxanthone template (3). These reactions showed very high catalytic turnovers, ca. 10^6 and 10^10 respectively, but this might simply mean that loss of catalyst through side reactions occurs only very slowly. However, the reactions also involve astonishing apparent effective molarities (EM's) of the catalysts.

At a concentration of 15 \times 10^{-9} M the catalyst 2, in a mixed complex, performs an essentially complete (>99%) selective chlorination on 15 mM 1 with 3 equiv of PhICl2. However, in control reactions under the same conditions uncomplexed aryl iodides such as 2 in the absence of MII+ or PhI itself in the presence of NiII, do not perform any intermolecular reaction (<4%) even at 15 mM aryl iodide. In such controls we begin to see random intermolecular attack only with 50 equiv of PhICl2 chlorinating


0002-7863/86/1508-6418$01.50/0 © 1986 American Chemical Society