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STEREOCHEMISTRY OF BF_3 CATALYZED METHANOLYSIS OF PHOSPHETANE AMIDES

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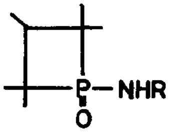
In the nucleophilic substitution at phosphoryl center of phosphetan-1-oxides, the rule of retention of configuration has been generally accepted since the suggestion by Trippett et al.1) However, recent report of Emsley et al2) disclosed an exceptional case in which inversion products were realized in the reaction of 2,2,3,4,4-pentamethyl-1-chlorophosphetan-1-oxide with several alcohols. Our continuing interest in the stereochemical study on the displacement reaction of phosphinamides3) led us to investigate the acid catalyzed methanolysis of N-benzyl and N-phenyl phosphetane amides (1a,b). This communication describes the result which not only provides an additional example of the violation of the retention rule but also indicates the applicability of the rule seems to be effected by the relative apicophilicity of the leaving groups and coordination property of the medium.



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Although both amides resisted to methanolysis in the presence of protic acid such as HCl, H_2SO_4, and CF_3COOH, by employing BF_3 of a Lewis acid the solvolysis did take place. When 1a($R=CH_2Ph$ trans, mp. 159-162°C4)) was treated with 1.3% BF_3 in methanol for 48 hrs under reflux, the corresponding methyl ester 2(trans, cis mixture) was obtained in a fair yield. The trans/cis ratio of the product was determined as 1.7 by NMR using $Eu(DPM)_3$5). That the ratio is due to kinetically controlled process was proved by the control experiments as indicated in Table 1; under the same reaction condition neither isomer interconversion nor exchange of CD_3O by CH_3O was observed.6)

Table 1. BF_3 Catalyzed Methanolysis of Methyl Ester **2**

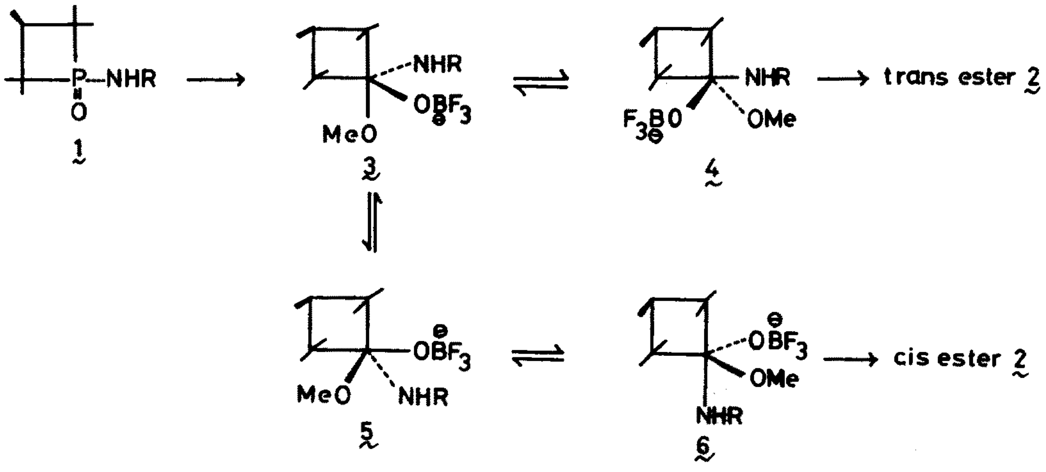
Starting Methyl Ester **2**	Reaction Time	t/c Ratio of Recovered **2**
2(OCH_3 trans only)	48 hr	trans only
2(OCH_3 trans/cis 1.9$_1$)	48 hr	trans/cis 1.98
2(OCD_3 trans only)	48 hr	no OCH_3 trans OCD_3 only
2(OCD_3 trans only)	12 day	no OCH_3 trans OCD_3 only
2(OCD_3 trans/cis 1.9)	16 day*	no OCH_3 trans/cis OCD_3 1.9

* In this case 1.1% BF_3 in MeOH was used , whereas 1.3% solutions were used in all other cases.

In order to see the effect of the leaving group on the trans/cis ratio of the product, N-phenyl phosphetane amide **1b**(R=Ph trans, mp. 172-173°C) was then subjected to methanolysis under the same condition. The reaction was too slow and even after refluxing for 17 days only a trace amount of the methyl ester was obtained with almost complete recovery of the starting trans amide **1b**. The trans/cis ratio in this case was higher than 5, indicating that the extent of the inversion depended on the character of the leaving groups.

The characteristic features observed in the above experiments could be explained by considering pentacoordinate intermediate mechanism, though the details of the mechanism await further study including kinetics, and the A-2 mechanism with some A-1 character could not be completely ruled out[7].

As shown in the chart, coordination of BF$_3$ with phosphoryl oxygen of the intermediate **3** makes its pseudorotation to **5** possible which is ordinarily prohibited, resulting in the inversion product, cis methyl ester **2**. The different inversion ratio observed in **1a** and **1b** could be ascribed to the relative apicophilicity of the substituents: higher apicophilic N-phenyl group renders the pseudorotation of **3** to **4** more favorable, compared with less apicophilic N-benzyl compound.



In conclusion we would suggest that the violation of the retention rule is not unusual and it may take place when the reaction condition is acidic in a sense that P-O$^-$ character decreases, and the ratio of retention/inversion seems to be dependent on the relative apicophilicity of the leaving groups compared to the acid conjugated P=O.

References and Notes

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6) It is of interest that the exchange of OCD_3 by OCH_3 with retention of configuration and without isomer crossover was observed in the basic condition(ref. 1b) but not in this acidic condition.

7) One of the authors(T.K.) previously investigated the acid catalyzed hydrolysis of N,N-dimethyl-2,2,3,4,4-pentamethyltrimethylenephosphinamide and suggested the direct displacement mechanism(A-2) on the basis of kinetic data. T. Koizumi, and P. Haake, J. Amer. Chem. Soc., **95**, 8073(1973).
However, there have been some arguments on the interpretation of the kinetic data and the mechanism of the hydrolysis seemed to require further study. J. R. Corfield, N. J. De'ath, and S. Trippett, J. Chem. Soc. Chem. Comm., **1970**, 1502.
At least in the present case it seems quite reasonable to consider the pentacoordinate intermediate mechanism because the better leaving anilino group (see ref. 3) gave higher retention/inversion ratio.