Isocyano-epoxide may be the organic functional moiety reported for the first time in organic chemistry as far as we know. Concerning biogenetic problem, we can see some relation to pentenomycins[7] and crotoepoxide.[8]

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Acid-Catalyzed Methanolysis of optically Active N-Cyclohexyl Methylphenylphosphinamide——A Stereochemical Evidence for A-2 Mechanism——

A stereochemical study of the acid-catalyzed methanolysis of N-cyclohexyl methylphenylphosphinamide shows that the reaction proceeds by almost pure A-2 mechanism irrespective of the acidity of the reaction medium.

One of the authors (T. K) previously suggested[1] that the acid-catalyzed hydrolysis of phosphinamides proceeds by a continuous spectrum of mechanisms ranging from direct nucleophilic substitution (A-2) mechanism to unimolecular dissociation (A-1) mechanism and the degree of blending of the two extremes depends on the nucleophilicity of the leaving groups and the substituents at phosphorus. Our recent finding[2] that the acid-catalyzed methanolysis of optically active methylphenylphosphinanilide (**1**) proceeds by the acidity dependent merged A-1 and A-2 mechanisms strongly supported the above concept from the stereochemical point of view. However, the lack of the stereochemical evidences for the existence of the two extreme cases (pure A-1 or pure A-2) still leaves the concept rather ambiguous, though there have been recent papers[3] suggesting A-2 mechanism from kinetic data only.

We would report here our result on the acid-catalyzed methanolysis of (+)-N-cyclohexyl methylphenylphosphinamide (**2**), which clearly indicates that the almost pure A-2 mechanism is operative in this case irrespective of the change of the acidity of the medium.

(S)-Menthyl methylphenylphosphinate prepared by the Nudelman's procedure[4] was treated with lithium salt of cyclohexylamine in benzene to yield N-cyclohexyl methylphenylphosphinamide (**2**) (mp 117.0—118.5° $[\alpha]_D = 53.0°$ (MeOH)[5]). The optical purity of **2** is considered

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[5] All compounds listed in this paper gave satisfactory elemental analysis and spectral data. Optical rotations were measured on a JASCO DIP-4 Automatic polarimeter and refer to solvent MeOH.

as 100% in analogy with the case of the phosphinanilide **1**.[4] The cyclohexylamide **2** (0.4—0.8 mM) was treated with methanolic H_2SO_4 with various acid concentrations at room temperature overnight. The product, methyl methylphenylphosphinate, was isolated by microdistillation almost quantitatively. The optical rotations of the methyl ester[6] are shown in Table I.

TABLE I. Acid-Catalyzed Methanolysis of (−)-(S)-N-cyclohexyl Methlphenylphosphinamide **2**

$[H^+]$ concentration (M)	$[\alpha]_D$ of methyl methylphenylphosphinate	$[H^+]$ concentration (M)	$[\alpha]_D$ of methyl methylphenylphosphinate
5.5×10^{-3}	−51.3°	2×10^{-1}	−50.4°
5×10^{-3}	−47.1°	$5 \times 10^{-}$	−50.4°
1×10^{-2}	−49.1°	1	−49.0°
5×10^{-2}	−48.8°	1.5	−49.9°
1×10^{-1}	−47.9°	9.2	−48.0°

Although there is a slight deviation in the observed values, the optical rotations are almost constant within experimental error, around −50°, regardless of the acidity of the reaction medium. DeBruin, *et al.* recently reported $[\alpha]_D = -52°$[7a] or $-56°$[7b] for (−)-(S)-methyl methylphenylphosphinate and our data fit fairly well with their values.[8]

In conclusion it is verified that the acid-catalyzed methanolysis of N-cyclohexyl methylphenylphosphinamide proceeds with almost complete (at least predominant) inversion of configuration irrespective of the acidity of the medium, which is in contrast with that of methylphenylphosphinanilide. The result together with our previous observations strongly supports the concept that the respective mechanisms of the acid-catalyzed solvolysis of phosphinamides may be characterized as pure A-2, merging A-2 and A-1, and pure A-1 and the degree of the merging depends on the leaving ability of amines (nucleophilicity of the leaving amine), the stability of the phosphinyl cations and the nucleophilicity of the solvents.

The validity of the above concept in the solvolysis of four membered phosphinamides (phosphetan amides) which has been used as a tool to distinguish mechanism[9] is now being investigated and will be reported elsewhere.

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6) The racemization of the ester is known to be negligible under the stronger acidic conditions. (ref. 2)

7) *a*) K.E. DeBruin and J.R. Petersen, *J. Org. Chem.*, 37, 2273 (1972); *b*) K.E. DeBruin and D.E. Perrin, *J. Org. Chem.*, **40**, 1523 (1975).

8) In ref. 2 we have estimated the value as −61° based on the $[\alpha]_D$ value of the anilide **1** prepared by the anilidation of the optically active methyl ester. It was then assumed that the anilidation reaction was a complete inversion process at the phosphoryl center. This assumption turned out to be incorrect when we have treated the same methyl ester ($[\alpha]_D$ −48.6°) with lithium cyclohexylamide under the same condition. The N-cyclohexyl phosphinamide **2** showed $[\alpha]_D = +1.2°$ indicating the reaction of methyl ester with lithium salt of amines is not always a complete inversion process and thus the previous value should be used with some modification. Although the above experiment may imply some importance for understanding the steric effect in the displacement at phosphoryl center, no further comments will be added in this communication.

9) P. Haake, R.D. Cook, T. Koizumi, P.S. Ossip, W. Schwarz, and D.A. Tyssee, *J. Am. Chem. Soc.*, **92**, 3828 (1970).