Acidity-dependent Merged Dissociative (*A*-1) and Associative (*A*-2) Mechanisms for Methanolysis of Methylphenylphosphinanilide

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Summary A stereochemical study of the acid-catalysed methanolysis of (−)-(*S*)-methylphenylphosphinanilide shows that the reaction proceeds by the acidity-dependent merged *A*-1 and *A*-2 mechanism.

RECENT papers by Tyssee *et al.*[1] and Harger[2] indicated that in the acid-catalysed hydrolysis of phosphinanilides three mechanisms can operate: *A*-2, *A*-1, and a merging of the *A*-1 and *A*-2 mechanisms, depending on the substituents on phosphorus and nitrogen. This is in contrast to the mechanism for phosphinamides,[3] which proceed by the *A*-2 mechanism. Lack of a definitive stereochemical study, however, leaves these mechanisms rather inconclusive.

We would report here our results on the methanolysis of (−)-(*S*)-methylphenylphosphinanilide under various acidic concentrations, which clearly indicate that both *A*-2 and *A*-1 mechanisms are operative for the reaction and further, the *A*-1 character increases with the acidity of the medium.

When the optically active methylphenylphosphinanilide[4] (*S*-form, $[\alpha]_D^{19}$ −32°, 100—200 mg) was treated with 10—50 ml of methanolic HCl or H_2SO_4 with various acid concentrations, at room temperature for 10—120 min, methyl methylphenylphosphinate was obtained in good yield after microdistillation. The optical rotations of the methyl ester are shown in Table. Clearly the optical rotations tend to decrease as the acidity of the medium increases.

TABLE. Acid-catalysed methanolysis of (−)-(*S*)-methylphenylphosphinanilide

$[H^+]$/M	$[\alpha]_D$ of product[a] (temp./°C)	Optical purity/%
7 × 10^{-3}[b]	−47·5 (10)	77·9
7 × 10^{-3}[b]	−46·0 (10)	75·4
0·1[b]	−43·5 (27)	71·3
0·7[b]	−36·7 (18)	60·2
1·4[b]	−32·5 (22)	53·3
1·4[b]	−35·5 (27)	58·2
3·8[c]	−30·4 (27)	49·8
5·6[c]	−29·8 (24)	48·9
9·4[c]	−24·3 (19)	39·8

[a] In MeOH. [b] With HCl. [c] With H_2SO_4.

When (−)-methyl methylphenylphosphinate ($[\alpha]_D^8$ −32·3°) was treated with lithium anilide in benzene, the anilide obtained showed $[\alpha]_D^8$ −17° which corresponds to 53% optical purity. Since the reaction of phosphinates with lithium anilide is known to take place with complete inversion,[4] the theoretical value for (−)-(*S*)-methyl methylphenylphosphinate is −61°. Based on this theoretical value, the optical purities of each product were calculated (Table). Since the amount of racemization of the methyl ester under the above conditions is negligible,† the results indicate that the acid-catalysed methanolysis of methylphenylphosphinanilide proceeds by the A-2 mechanism with some A-1 character (merged A-1 and A-2 mechanism) even under very dilute acidic conditions and the A-1 character increases with the acidity of the medium. No complete racemization (100% A-1 mechanism) was observed even in a very strong acidic solution.

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† When the methyl ester with $[\alpha]_D$ $-32\cdot3°$ was treated with $3\cdot5$M HCl–MeOH for 24 h at room temperature, the optical rotation of the recovered ester was unchanged.

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