group by alkaline hydrolysis after the methylation of **2** by dimethyl sulfate, giving 3-oxo-1,2,5-trimethyl-3H-pyrido[4,3-*b*]indole (**3**) as a major product.

The ultraviolet, fluorescence and excitation spectra of II were similar to those of I (or **2**). Those of III were very different from those of I or II.

In summary, one of the binding sites of activated Trp-P-2 to DNA is the 8-position of guanine in DNA. It is quite plausible that the activated form of Trp-P-2 is the corresponding hydroxylamine or its ester. N^2-oxide would be an alternative activated form. We are trying to identify II and III, and to get information on the structure of the modified DNA by amino-dipyridoimidazoles,[6] potent mutagens isolated from glutamic acid pyrolysate.

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Behaviour of S-Substituted Cysteine Sulfoxide under Acidolytical Deprotecting Conditions

Treatment of S-*p*-methoxybenzylcysteine sulfoxide with hydrogen fluoride or methanesulfonic acid in the presence of anisole afforded S-*p*-methoxyphenylcysteine as a major product, while S-benzylcysteine sulfoxide resisted to the action of these deprotecting reagents in peptide synthesis. Thiophenol was found to be a powerful reducing reagent of the sulfoxides.

Keywords——S-*p*-methoxybenzylcysteine sulfoxide; S-benzylcysteine sulfoxide; hydrogen fluoride deprotection; methanesulfonic acid deprotection; sodium in liquid ammonia reduction; S-*p*-methoxyphenylcysteine; thiophenol reduction of sulfoxides

In 1977, Live *et al.*[1] mentioned briefly the reduction of the sulfoxide of Cys(S-*p*-methylbenzyl) residue by acetone treatment in hydrogen bromide-acetic acid in the course of the solid phase synthesis of oxytocin. Little is known about the chemical nature of the sulfoxide of S-substituted cysteines, such as Cys(MBzl) and Cys(Bzl) [MBzl=S-*p*-methoxybenzyl, Bzl=S-benzyl], in peptide synthesis. Behaviour of these sulfoxides under acidolytical deprotecting conditions was examined.

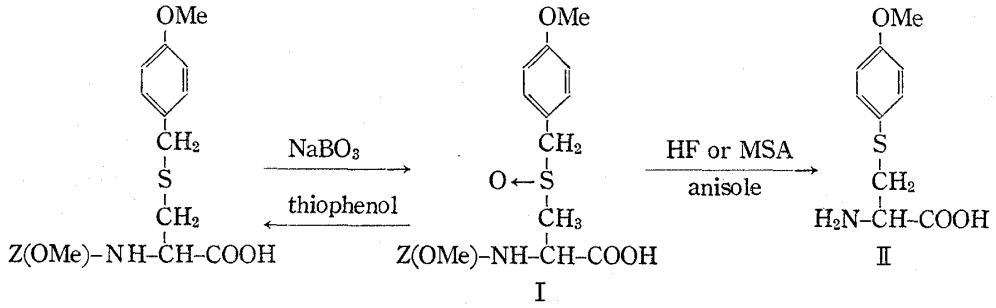
Oxidation of Z(OMe)-Cys(MBzl)-OH [Z(OMe)=*p*-methoxybenzyloxycarbonyl] by sodium perborate gave the corresponding sulfoxide (I) [mp 148—151°, $[\alpha]_D^{22}$ −72.8° in DMF. *Anal.* Calcd. for $C_{20}H_{23}NO_7S$: C, 56.99; H, 5.50; N, 3.32. Found: C, 56.89; H, 5.53; N, 3.33] quantitatively. The product seems to be a mixture of two diastereoisomers concerning the configuration of the sulfoxide grouping, as predicted by the similar oxidation of N^{α}-protected meth-

1) D. H. Live, W. C. Agosta and D. Cowburn, *J. Org. Chem.*, **42**, 3556 (1977).

ionine derivatives.[2] The sulfoxide (I) could be converted to cysteine by reduction with sodium in liquid ammonia, but not by acidolytical deprotecting reagents, such as hydrogen fluoride[3] or methanesulfonic acid (MSA).[4] When the sulfoxide (I) was treated with these acids in the presence of a cation scavenger, anisole, recovery of cysteine was unsatisfactory, giving S-*p*-methoxyphenylcysteine (II) [mp 189—190°, $[\alpha]_D^{22}$ +10.6° in 50% AcOH. *Anal.* Calcd. for $C_{10}H_{13}NO_3S$: C, 52.84; H, 5.77; N, 6.16; S, 14.11. Found: C, 53.12; H, 5.90; N, 5.93; S, 13.83] predominantly in both cases. This compound (II) emerged from the short column of an amino acid analyser at the retention time of 38 minutes.

The sulfoxide of Z(OMe)-Cys(Bzl)-OH [mp 161—163°, $[\alpha]_D^{22}$ −19.8° in DMF. *Anal.* Calcd. for $C_{19}H_{21}NO_6S$: C, 58.30; H, 5.41; N, 3.58. Found: C, 58.06; H, 5.35; N, 3.60] similarly prepared regenerated cysteine by reduction with sodium in liquid ammonia, like (I). Differently from the sulfoxide (I), this sulfoxide resisted to the action of hydrogen fluoride or MSA, giving the N^{α}-deprotected sulfoxide as a major product, even in the presence of a reasonable amount of anisole.

Formation of S-*p*-methoxyphenylcysteine (II) from the sulfoxide (I) may be accounted as the result of the substitution reaction initiated by protonation of the oxygen atom of the sulfoxide followed by hydrolysis. Different behaviour of the sulfoxide of Cys(Bzl) seems due to subtle difference of stabilities between the benzyl cations with or without the electron donating substituent at the paraposition.



The content of the sulfoxide in synthetic peptides may be estimated by the unusual presence of cysteic acid in acid hydrolysates. Above experimental results indicated that the sulfoxide of S-substituted cysteine residue, if any, should be reduced, before deprotection with hydrogen fluoride or MSA. As far as we tested, thiophenol seems to be a powerful reducing reagent for this purpose.

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