Br(OC)₃Re FRAGMENT AS A NEW PROTECTIVE GROUP IN PEPTIDE SYNTHESIS

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We have established that $fac-Br(OC)_{3}Re(NH_{2}CHRCO_{2}H)_{2}$ complexes (I) obtained by the replacement of a CO group in $BrRe(CO)_{5}$ by an amino acid [1] are capable of reacting with amino acid esters to form bis-dipeptide compounds (II)-(IV)

$$(I) + 2NH_{2}CHR'COOEt \rightarrow fac -Br(OC)_{3}Re(NH_{2}CHRCO-NHCHR'COOEt)_{2}$$
$$(II)-(IV)$$
$$R=H, R'=Me (II); R=CH_{2}Ph, R'=CH_{2}$$
$$(III); R=CH_{2}Ph, R'=Me (IV).$$
$$H$$

The condensation of (I) and amino acid esters were carried out in $CHCl_3$ at about 20°C by the carbodiimide method [2] using dicyclohexylcarbodiimide and N-hydroxysuccinimide (in 1:2 mole ratio) as activating agents. The thermal stability, solubility, and spectral indices of oily complexes (II)-(IV) are similar to those of starting compounds (I) and these complexes were isolated by our previous method [3] in 70-90% yields and characterized by elemental analysis and IR and PMR spectroscopy.

The deblocking of the amino groups and elimination of the free esters of the dipeptides from complexes (II)-(IV) may be achieved by treatment with Lewis bases such as pyridine or PPh₃ which are stronger than the amino acid or peptide. The action of pyridine on these compounds at 20-40°C leads to cleavage of both Re-NH₂ bonds and removal of the protective group as the fac-Br(OC)₃Re(NC₅H₅)₂ complex independently of the structure of the dipeptide ligand. The yields of the dipeptide esters reach 95%.

The reaction with PPh₃ is more complex and its course is dependent on the structure of the peptide ligands. Thus, heating of (III) and PPH₃ in $CHCl_3$ at 60°C leads to the elimination of two dipeptide ester molecules, while the protective group is removed as mer,trans-Br(OC)₃Re(PPh₃)₂. Under analogous conditions, only one peptide ligand is replaced in sterically less hindered (IV) to form a chelate which has very limited solu-

bility in polar solvents, $(Ph_3P)_2(OC)_2Re-NH_2CH(CH_2Ph)CO-NHCH(Me)COO^{1}CHCl_3$. This derivative decomposes at 243-245°C. IR spectrum in KBr (v, cm⁻¹): 1925 s, 1845 s (C=O), 1636 m (CONH), 1615 m, 1428 w (CO₂).

These reactions are the first example of the use of a metal carbonyl fragment for the protection of the NH_2 group in amino acids in peptide synthesis.

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