4-Methylpyrazole-3-^3H oxalate. 4-Methyl-3-iodo-pyrazole (213 mg, 1.03 mmole) prepared according to Hüttel *et al.*[7] was dissolved in 1.5 ml of 90 % ethanol containing 60 mg of NaOH (1.5 mmole). Palladium on charcoal catalyst (10 %, 20 mg) was added and the mixture was vigorously stirred in a hydrogen-tritium mixture (37 Ci T_2) in a vacuum tritiation apparatus. The reaction was complete within 15 min. Unreacted tritium (about 10 Ci, diluted with H_2) was recovered by trapping on activated uranium powder. The catalyst was removed by filtration and washed several times with ethanol. The filtrate was evaporated to dryness *in vacuo*, the residue was extracted with ether. The ethereal solution was evaporated to a small volume (about 5 ml) and a solution of anhydrous oxalic acid (100 mg) in 10 ml of ether was added. The oxalate of the 4-methyl-3-^{3}H-pyrazole was collected and washed with ether three times. Yield 60 mg. This product was diluted with 100 mg of inactive 4-methyl-pyrazole oxalate and recrystallized from methanol-ether. Yield 150 mg; m.p. 155.5–156°C (uncorr.); spec. act. 14.7 mCi/mg=2.5 Ci/mmole; activity yield 8.7 %.

The product showed a single radioactive peak (R_F =0.21) on silica thin layer plate (Merck F-254) developed with chloroform-methanol (95:5), which corresponds to the spot of the reference standard, which was made visible by exposing the chromatogram to iodine vapours.

Radioactivity measurements. The radioactivity of the products was measured in a Packard liquid scintillation spectrometer (Model 3320) using internal standardization (Hexadecane-1,2-^{3}H). Scanning of the chromatogram was made in a Packard radiochromatogram scanner (Model 7200).

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Note on the Use of Active Esters in Combination with 1,2,4-Triazole in Solid Phase Peptide Synthesis

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In a series of papers,[1–4] Beyerman and co-workers advocated the use of bifunctional catalysts in the synthesis of peptides with the aid of active esters. This procedure was later extended by the same school [5,6] to solid phase peptide synthesis [7] (SPPS).

Since at the present state of SPPS, active esters, especially *p*-nitrophenyl esters, are generally used for incorporation of asparagine and glutamine, we recently did a quantitative study [8] of the reactivity of such an ester towards amino acids fixed to a resin. This communication reports some further experiments of the same kind wherein we have investigated the use of 1,2,4-triazole as a catalyst for the coupling reaction. Since preliminary experiments with *t*-butyloxycarbonyl-L-asparagine *p*-nitrophenyl ester (Boc-L-Asn-ONp) did not reveal any accelerating effect (Table 1), we also studied a few other active esters. In no case have we observed any improvement in coupling efficiency in the presence of triazole.

Table 1. Coupling experiments [a] with Boc-L-Asn-ONp and L-Leu-L-Ala-polymer with addition 1,2,4-triazole.

Experiment No.	Reaction time h	Yield (%) I	Yield (%) II	Yield [8] without triazole %
1	1	64	60	70
2	5	82	78	90
3	17.5	94	96	99.6

[a] Detailed reaction conditions are found under Procedure and results.

For the final experiments four active esters of Boc-L-Phe were used: *p*-nitrophenyl (—ONp), pentachlorophenyl (—PCP), *N*-hydroxysuccinimide (—OSu),

and cyanomethyl ($-OCH_2CN$). The experiments performed are summarized in Table 2. The data show that the —ONp and —OSu esters do not respond to triazole addition at all, and in the case of the —PCP ester the coupling yield is slightly decreased.

Table 2. Coupling experiments [a] with Boc-L-Phe active ester (X) [b] and L-Ala-polymer.

Experiment No.	Active ester (X)	1,2,4-Triazole added	Reaction time h	Yield (%) I	II
4	-ONp	No	2	59	61
5	»	Yes	2	60	63
6	-PCP	No	2	70	67
7	»	Yes	2	65	62
8	-OSu	No	2	97	96
9	»	Yes	2	96	97
10	$-OCH_2CN$	No	64	32	35
11	»	Yes	64	32	34

[a] See Table 1. [b] For abbreviations, see text.

Since catalysis by triazole is best documented with cyanomethyl ester,[1,2,4] we decided finally to try such an ester as well. Not even with a cyanomethyl ester (*cf.* experiments 10 and 11), however, were we able to detect any catalytic effect of 1,2,4-triazole.

In a recent paper,[9] kinetic measurements in solution on aminolysis of Z-L-Phe-ONp (Z=benzyloxycarbonyl) were described. The catalytic effects of several compounds including 1,2,4-triazole were investigated. Under the conditions used, triazole had a small accelerating effect.

Procedure and results. Boc-L-Asn-ONp, Boc-L-Phe-ONp, Boc-L-Phe-PCP, and Boc-L-Phe-OSu were prepared according to published procedures. Physical constants agreed well with reported ones.

Boc-L-Phe-OCH_2CN was prepared according to the procedure for tritylglycine cyanomethyl ester.[10] M.p. 62.5—63.5°, $[\alpha]_{589}^{25}$ —20.3°, $[\alpha]_{578}^{25}$ —21.2° (c=2.05, ethyl acetate.) (Found: C 63.15; H 6.68; N 9.20. Calc. for $C_{16}H_{20}N_2O_4$: C 63.14; H 6.62; N 9.20).

Solvent. All coupling reactions were performed in DMF that had been dried over a molecular sieve (Union Carbide, type 4A). The amine content was checked with 2,4-dinitrofluorobenzene according to Ref. 11.

Polymers. These were identical with the ones used in our earlier work.[8] 1,2,4-Triazole was prepared according to Ref. 12. It gave a satisfactory C,H,N analysis. Molecular weight: 69 (mass spectrum).

Coupling experiments and subsequent determinations. All coupling experiments were performed in duplicates at room temperature (20—25°C). The experimental procedure was as described earlier.[8] In all experiments with 1,2,4-triazole, 5 equiv. of that compound was added. 5 equiv. of Boc-L-Asn-ONp and 4 equiv. of Boc-L-Phe ester were used.[5,6]

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