

SYNLETT Spotlight 255

DEAD/DIAD – More than Simple Mitsunobu Reagents

Compiled by Arthur Eugen Kümmerle



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

Diethyl azodicarboxylate (DEAD) and diisopropyl azodicarboxylate (DIAD) (Figure 1), are widely used reagents in organic synthesis.

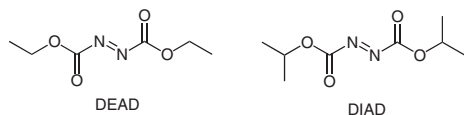
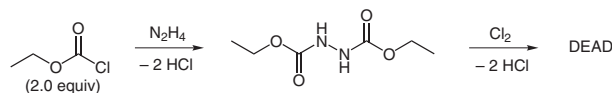


Figure 1

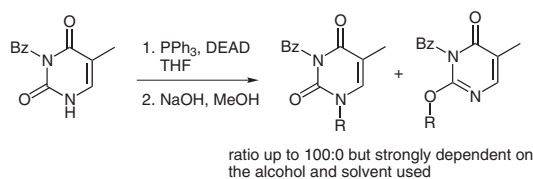
These are important reagents in the Mitsunobu reaction,^{1,2} which is a versatile and widely used method for the dehydrative coupling of an alcohol with clean stereogenic inversion and is perhaps the most favorable reaction to invert chiral centers of secondary alcohols.^{1,2} This kind of reaction can also be applied in aminations, cyclodehydrations, deoxygenations, and in dehydrative alkylations.³

Abstracts

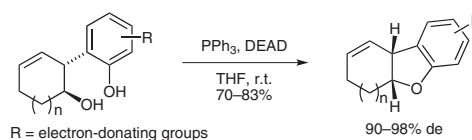
(A) Alkylation can be achieved under Mitsunobu conditions (DEAD + PPh₃). This reaction is an important tool in carbocyclic nucleoside chemistry for the direct coupling of alcohols with heterocycles. Ludek and Meier described the influence of the solvent^{6a} and the alcohol^{6b} utilized on *N*- vs. *O*-alkylation of *N*3-benzoylthymine.



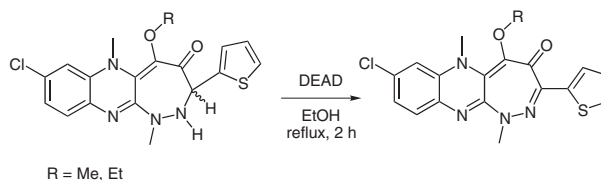
Scheme 1



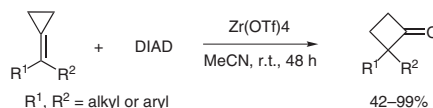
(B) The Mitsunobu reaction can be used to induce cyclodehydration from hydroxyphenols in good yield and diastereoisomeric excess, giving a new and easy access to cycloalkenobenzofurans.⁷



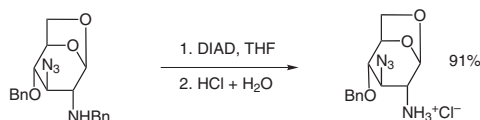
(C) DEAD can be utilized as dehydrogenation agent as demonstrated in its reaction with 5-alkoxy-8-chloro-2,3,4,6-tetrahydro-1-methyl-4-oxo-3-(2-thienyl)-1*H*-1,2-diazepino[3,4-*b*]quinoxaline compounds to give 5-alkoxy-8-chloro-4,6-dihydro-1-methyl-4-oxo-3-(2-thienyl)-1*H*-1,2-diazepino[3,4-*b*]quinoxaline compounds.⁸



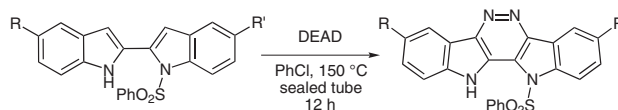
(D) Cyclobutanone ring-expansion products were obtained in moderate to high yields by treatment of methylenecyclopropanes with DIAD or DEAD in acetonitrile under mild conditions in the presence of a Lewis acid such as Zr(OTf)₄.⁹



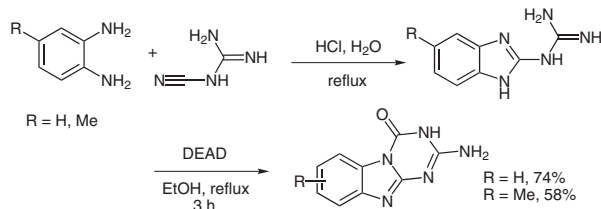
(E) The selective N-debenzylation of benzylamines with DIAD in THF was achieved in the presence of azido-, *O*-benzyl, and *N*-tosyl groups in reactions of benzylamines derived from 1,6-anhydro-β-*D*-glucopyranose.¹⁰



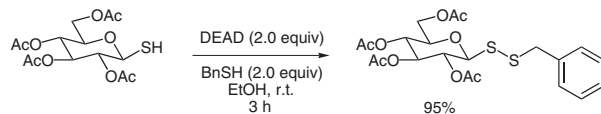
(F) Formal [4+2] cycloadditions were performed by reaction of symmetrically substituted 2,2'-biindole compounds with DEAD to provide 5,5'-dichloroindigo azine derivatives.¹¹



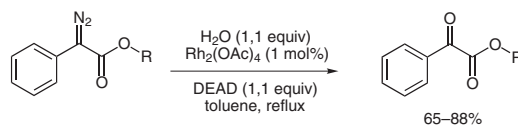
(G) The heterocycle ring construction of 2-amino-*s*-triazino[1,2-*a*]benzimidazole from 2-guanidinobenzimidazoles was produced by a ring annelation reaction with DEAD in EtOH.¹²



(H) DEAD is an efficient reagent in the production of disulfides. A one-pot procedure employing mild conditions was described in which a series of glycosyl disulfides were synthesized in excellent yields.¹³



(I) The reaction of aryl diazoacetates with H₂O and DEAD catalyzed by dirhodium acetate gives aryl α-keto esters in high yields.¹⁴



References

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