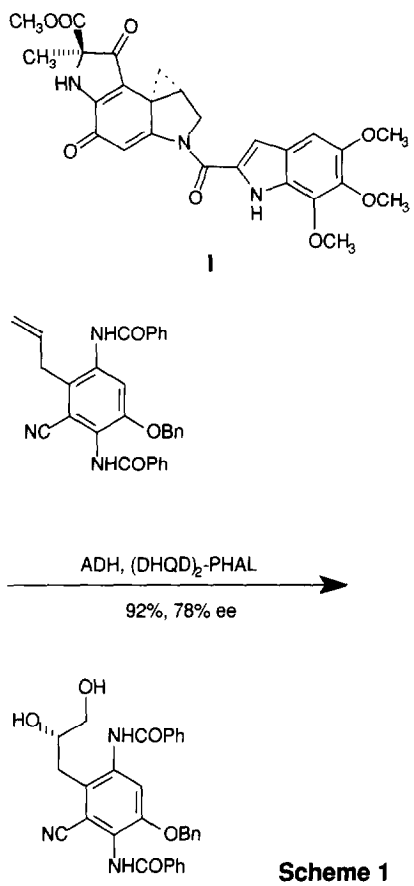
Enantioselective total synthesis of (+)-duocarmycin A

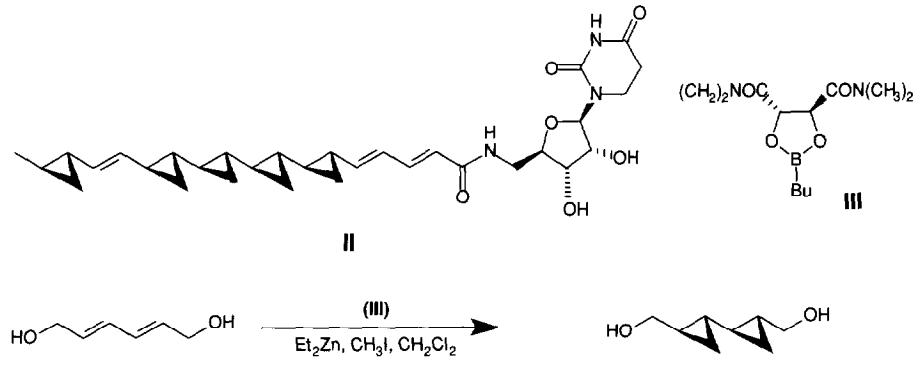
Duocarmycin A **I** is representative of a class of naturally occurring potent antitumour antibiotics that alkylate specific sequences of duplex DNA. Boger, D.L. and coworkers [*J. Am. Chem. Soc.* in press] describe the first enantioselective total synthesis of (+)-duocarmycin A, epi-(+)-duocarmycin A and their unnatural enantiomers. The synthesis also includes the first reported example of a Sharpless asymmetric dihydroxylation reaction, which gives the opposite configuration to that predicted from established models (Scheme 1).



Scheme 1

Total synthesis of antifungal FR-900848

FR-900848 **II** is a potent antifungal nucleoside isolated from *Streptoverticillium fervans* and is selectively active against filamentous fungi, such as *Aspergillus niger*. Barrett, A.G.M. and Kasdorf, K. [*Chem. Commun.* (1996) 325–326] describe the total synthesis of this agent using the asymmetric cyclopropanation methodology recently reported by Charette, A.B. and Juteau, H. [*J. Am. Chem. Soc.* (1994) 116, 2651–2652] (Scheme 2) to control the stereochemistry at the ten stereocentres with the chiral auxillary **III**.



Scheme 2

Selective cleavage of ketals and acetals

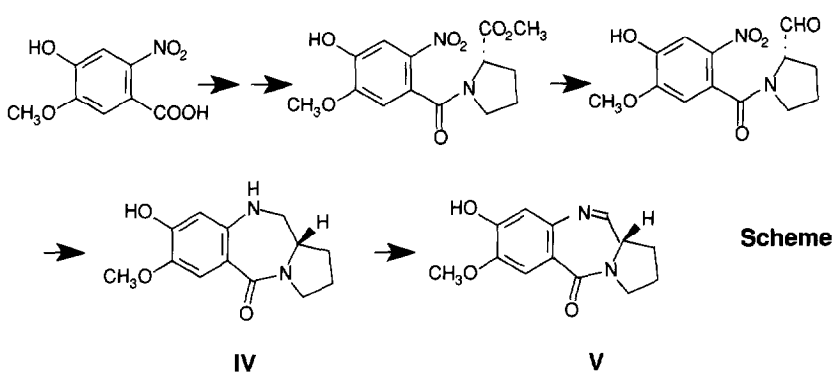
The deprotection of 1,3-dioxolane ketals and acetals is usually accomplished using acid hydrolysis. However, such an approach is problematic for compounds containing acid-sensitive functional groups. Johnstone, C., Kerr, W.J. and Scott, J.S. [*Chem. Commun.* (1996) 341–342] report an alternative approach for the selective cleavage of ketals and acetals under neutral, anhydrous conditions using triphenylphosphine and carbon tetrabromide. Examples demonstrated that this approach may be used to deprotect aromatic, α,β-unsaturated and aliphatic ketals and aromatic and α,β-unsaturated acetals in either dichloromethane or tetrahydrofuran.

Synthesis of pyrrolo [2,1*c*][1,4]benzodiazepie antibiotics

The pyrrolo[2,1-*c*][1,4]benzodiazepine DNA-binding antitumour antibiotics is an important class of agents produced by various *Streptomyces* species and includes anthramycin, tomaymycin and DC-81 **V**. Kamal, A. and Rao, N.V. [*Chem. Commun.* (1996) 385–386] report a new approach to the synthesis of these imine containing pyrrolo[2,1-*c*][1,4]benzodiazepine using the mild oxidation of the cyclic secondary amine **IV** with activated dimethylsulphoxide (Scheme 3). This approach avoids the use of protective and deprotective steps and ensures the stereochemical integrity of the chiral centre at the C-11a position.

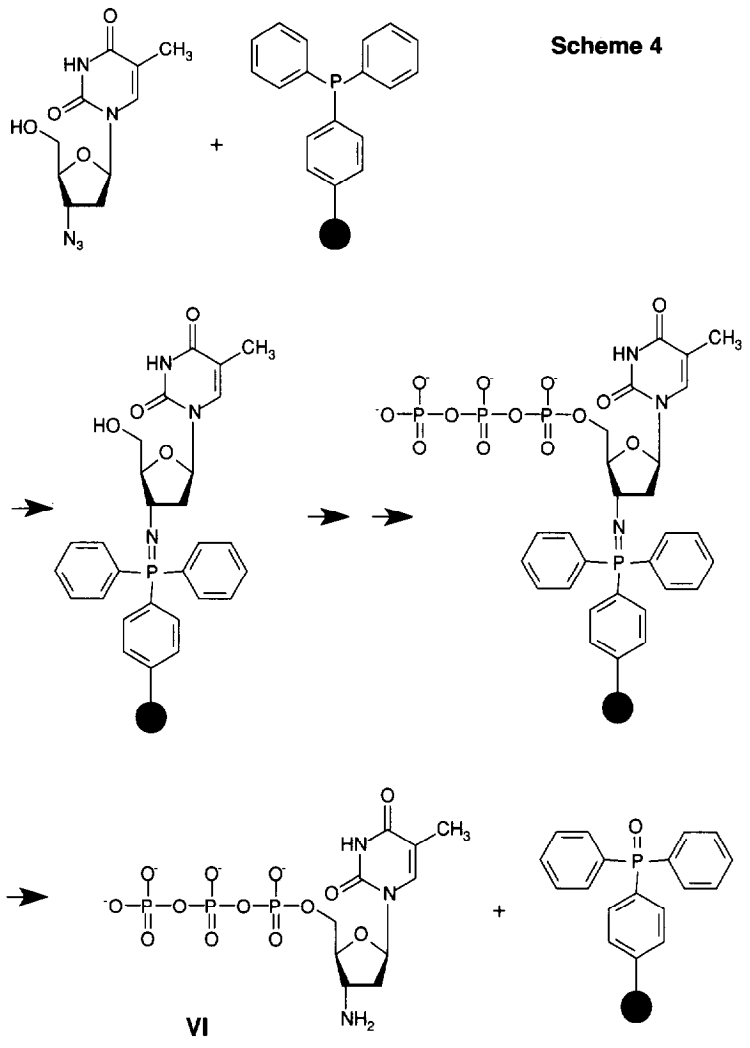
Solid-phase synthesis of 2′ and 3′-amino-nucleoside triphosphates

The 2′ and 3′-amino functionalized nucleoside 5′-triphosphates have application as



Scheme 3

Scheme 4



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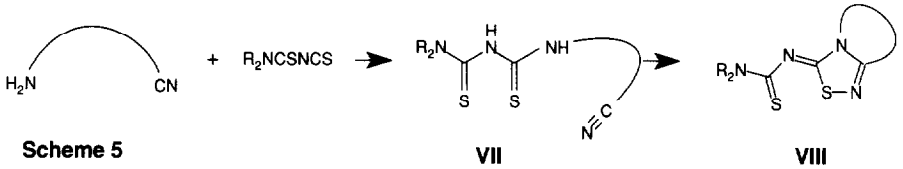
terminators for DNA and RNA sequencing and for studying the mechanisms of ribozymes. The resistance of these nucleosides to degradation by nucleases also makes them attractive for the synthesis of modified RNA and DNA sequences as antisense oligonucleotides. Schoetzau, T., Holletz, T. and Cech, D. [*Chem. Commun.* (1996) 387–388] describe the use of a solid-support approach for the rapid synthesis of these amino 5′-triphosphate nucleosides, such as **VI**, using a polymer-bound triphenylphosphine (Scheme 4). As the azidonucleosides are bound to the support through a stable phosphinimine linkage, chemical manipulations to the nucleoside can be conducted whilst it is still attached to the polymer.

Synthesis of fused 1,2,4-thiadiazoles

L'abbé, G., D'hooge, B. and Dehaen, W. [*J. Chem. Soc., Perkin Trans. I*(1996) 225–226] describe the synthesis of fused 1,2,4-thiadiazoles **VIII** from cyano-substituted amines and thiocarbamoyl isothiocyanates by oxidation of the intermediate dithiobiurets **VII** (Scheme 5). This approach may have application for the preparation of a wide range of fused 1,2,4-thiadiazoles for screening using linear combinatorial synthesis.

Scheme 5



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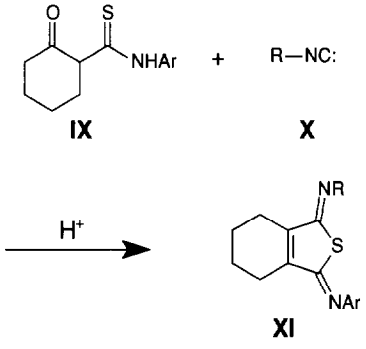
Synthesis of benzo[*c*]-thiophenes

Bossio, R. and coworkers [*J.Chem. Soc., Perkin Trans. I* (1996) 229–230] describe the synthesis of 1-arylimino-3-(*N*-substituted imino)-1,3,4,5,6,7-hexahydrobenzo-[*c*]thiophens **XI** using a single-pot reaction between 2-(arylaminothiocarbonyl)cyclohexanes **IX** and isocyanides **X** under acidic conditions (Scheme 6). This hitherto unknown class of diimino thioanhydrides may be useful as dienophiles in Diels–Alder reactions.

Scheme 6

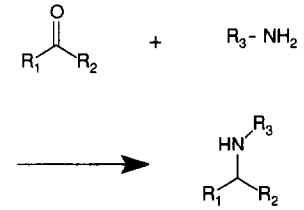


IX X XI

Preparation of secondary amines

Mićović, I.V. and coworkers [*J.Chem. Soc., Perkin Trans. I* (1996) 265–269] describe a novel and efficient approach to the preparation of secondary amines by reductive amination of carbonyl compounds with primary amines (Scheme 7). The process involves the use of metallic magnesium in methanol, as the reducing agent, in the presence of a triethylamine-acetic acid buffer.

Scheme 7



R_1 = alkyl, R_2 = H,alkyl, R_3 = H,alkyl,aryl