

This article was downloaded by:

On: 26 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

A New Protecting Group Strategy for Amino Groups in Oligonucleotide Chemistry: CEOC Group

Muthiah Manoharan^a; Thazha P. Prakash^a; Isabelle Barber-peoc'h^a; Balkrishen Bhat^a; Guillermo Vasquez^a; Bruce S. Ross^a; P. Dan Cook^a

^a Department of Medicinal Chemistry, Isis Pharmaceuticals, Carlsbad, CA, USA

To cite this Article Manoharan, Muthiah , Prakash, Thazha P. , Barber-peoc'h, Isabelle , Bhat, Balkrishen , Vasquez, Guillermo , Ross, Bruce S. and Cook, P. Dan(1999) 'A New Protecting Group Strategy for Amino Groups in Oligonucleotide Chemistry: CEOC Group', *Nucleosides, Nucleotides and Nucleic Acids*, 18: 6, 1199 – 1201

To link to this Article: DOI: 10.1080/07328319908044661

URL: <http://dx.doi.org/10.1080/07328319908044661>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

A NEW PROTECTING GROUP STRATEGY FOR AMINO GROUPS IN OLIGONUCLEOTIDE CHEMISTRY: CEOC GROUP

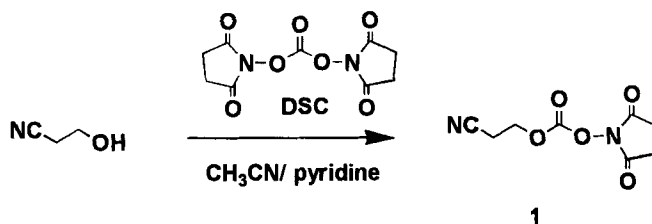
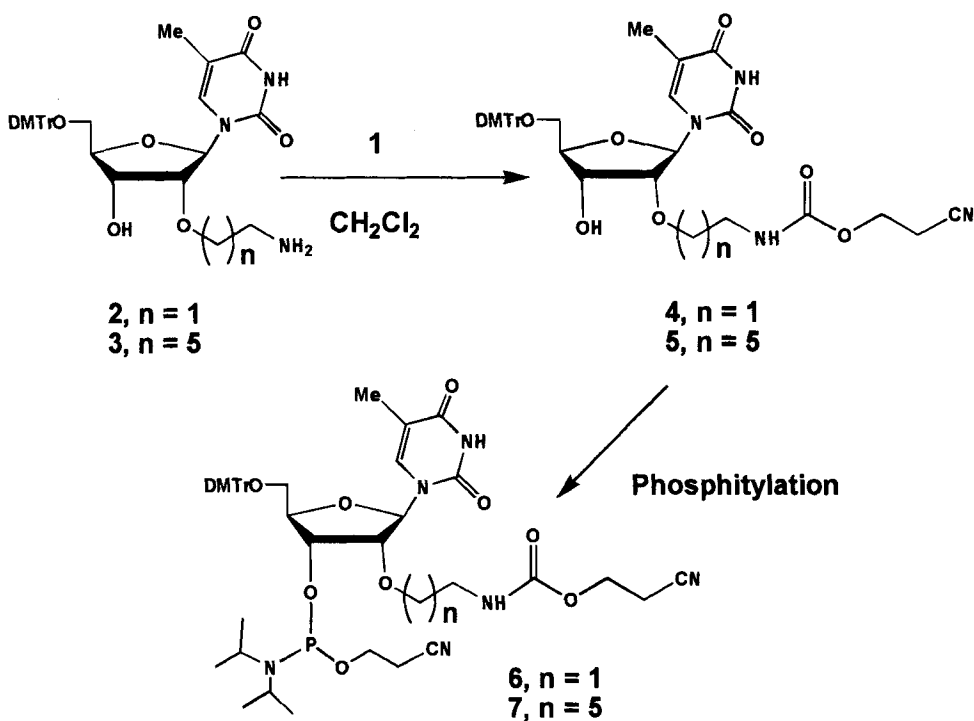
Muthiah Manoharan, Thazha P. Prakash, Isabelle Barber-Peoc'h, Balkrishen Bhat,
Guillermo Vasquez, Bruce S. Ross and P. Dan Cook

Department of Medicinal Chemistry, Isis Pharmaceuticals, 2292 Faraday Avenue,
Carlsbad, CA 92008 USA

SUMMARY: A new protecting group, 2-cyanoethyloxycarbonyl, or CEOC, has been developed for amino groups and utilized in synthesizing modified oligonucleotides. (CEOC)-oxy-succinimide reagent has been synthesized to introduce this protecting group. The protecting group is removed by standard oligonucleotide deprotection protocols. Using this approach, oligonucleotides have been synthesized with various types of alkylamine substituents.

During oligonucleotide synthesis, convenient amino group protection methodology is important not only for exocyclic amines but also useful for side chain amino groups ("aminolinkers" or "aminotethers"). Conjugation of different ligands to improve the properties of oligonucleotides requires placement of protected amino groups with appropriate tethers in the appropriate building blocks and synthesizing oligonucleotides.

Our goal to make a convenient reagent for cyanoethyloxycarbonylation reagent resulted in cyanoethyloxycarbonyloxy succinimide (CEOC succinimide), a stable crystalline compound that can be synthesized from readily available commercial chemicals. In addition to the potential applications in the nucleic acid field, this reagent can also be of general use for amino groups in all classes of compounds. CEOC succinimide **1** was generated from reacting 2-cyanoethanol with disuccinimidyl carbonate (DSC) ¹⁻³ in acetonitrile in the presence of pyridine to yield CEOC succinimide (**Scheme 1**).

Scheme 1**Scheme 2**

The CEOC group was used in protecting amino groups in nucleosides building blocks according to **Scheme 2**. The phosphoramidites **6** and **7** were used in standard oligonucleotide synthesis; subsequently, standard deprotection conditions (concentrated ammonium hydroxide, 12 hrs) were used to deprotect the oligomers. The CEOC groups were removed without any side products in oligomers having all four nucleobases. In summary, a convenient solid reagent to protect aminolinkers (CEOC-oxy-succinimide) has

been developed and used to protect nucleoside-based 2'-amino linkers and non-nucleosidic aminolinkers. After oligonucleotide synthesis on containing these aminolinkers, standard NH_4OH treatment removes the CEOC group by β -elimination. The resultant oligonucleotides with 2'-*O*-alkylamines stabilize antisense oligomers toward RNA binding. The aminolinkers generated by this new method are also useful for conjugation chemistry.

REFERENCES

- 1 Ghosh, A. K.; Duong, T. T.; McKee, S. P.; Thompson, W. J. *Tetrahedron Lett.* **1992**, 33, 2781.
- 2 Ghosh, A. K.; Duong, T. McKee, S. P. *Tetrahedron Lett.* **1991**, 32, 4251.
- 3 Ogura, H.; Kobayashi, T.; Kawabe, K.; Takeda, K. *Tetrahedron Lett.* **1975**, 4745.