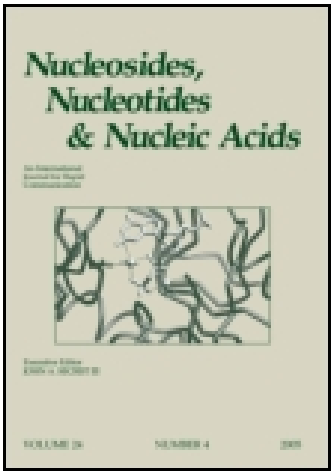

Nucleosides and Nucleotides
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn19

New Photolabile Protecting Groups of the 2-(2-Nitrophenyl)ethoxycarbonyl- and the 2-(2-Nitrophenyl)ethylsulfonyl-Type for the Oligonucleotide Synthesis

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Published online: 04 Oct 2006.

To cite this article: S. Bühler , H. Giegrich & W. Pfleiderer (1999) New Photolabile Protecting Groups of the 2-(2-Nitrophenyl)ethoxycarbonyl- and the 2-(2-Nitrophenyl)ethylsulfonyl-Type for the Oligonucleotide Synthesis, Nucleosides and Nucleotides, 18:6-7, 1281-1283, DOI: 10.1080/07328319908044692

To link to this article: http://dx.doi.org/10.1080/07328319908044692

NUCLEOSIDES & NUCLEOTIDES, 18(6&7), 1281–1283 (1999)

NEW PHOTOLABILE PROTECTING GROUPS OF THE 2-(2-NITROPHENYL)ETHOXYCARBONYL- AND THE 2-(2-NITROPHENYL)ETHYLSULFONYL-TYPE FOR THE OLIGONUCLEOTIDE SYNTHESIS

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ABSTRACT: New photolabile blocking groups have been synthesized and introduced into the 5'-OH position of thymidine. The 5'-O-protected thymidines were irradiated at 365 nm under identical conditions and the half-lives and thymidine yields were determined to investigate the influence of different substituents in the two corresponding series.

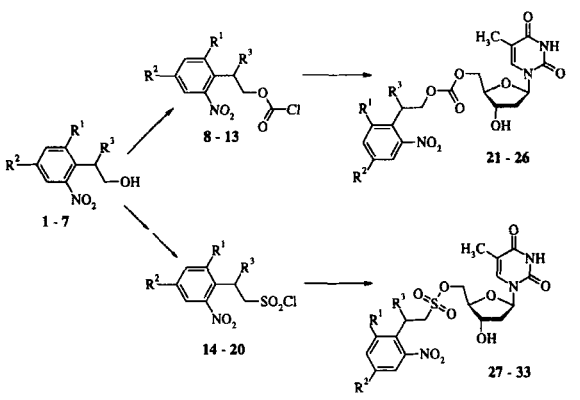
Light-directed synthesis of oligonucleotides permits the preparation of thousands of different sequences at small location. These DNA chips are a rapid and inexpensive tool in sequencing of DNA. Therefore, a great need of very efficient photoremovable protecting groups exists, however, the photochemical deprotection still results in lower yields compared to acid deprotection.

The preparation of the protecting group reagents could be achieved in one (carbonyl series)[1] or two (sulfonyl series)[2-5] steps starting from the corresponding alcohols[6-7] (Scheme 1).

The introduction of the new blocking groups into the 5'-OH position of thymidine was carried out in pyridine/CH_2Cl_2 1:1 at low temperature.

The photochemical half-lives t_H and thymidine yields (table 1) of the 5'-O-protected thymidine derivates were determined by irradiation with a 200 W mercury lamp (365 nm, methanol/water 1:1), followed by HPLC analysis . The half-lifes were calculated

SCHEME 1



Compound	R^1	R^2	R^3
1, 8, 14, 21, 27	H	H	H
2, 9, 15, 22, 28	Cl	H	H
3, 16, 29	H	Cl	H
4, 10, 17, 23, 30	H	H	CH_3
5, 11, 18, 24, 31	H	Cl	CH_3
6, 12, 19, 25, 32	H	Br	CH_3
7, 13, 20, 26, 33	H	I	CH_3

TABLE 1: Photolysis data of 5'–O–protected thymidines

Substituents			Carbonate–Series			Sulfonate–Series		
R^1	R^2	R^3		t_H	Yield thymidine		t_H	Yield thymidine
H	H	H	**21**	7.5 min	80 % (60 min)	**27**	10.9 min	43 % (90 min)
Cl	H	H	**22**	82 min	80 % (60 min)	**28**	16.3 min	18 % (2 h)
H	Cl	H	—			**29**	10.9 min	36 % (2 h)
H	H	CH_3	**23**	56 s	76 % (10 min)	**30**	82 s	43 % (10 min)
H	Cl	CH_3	**24**	62 s	85 % (10 min)	**31**	66 s	60 % (10 min)
H	Br	CH_3	**25**	60 s	85 % (10 min)	**32**	70 s	63 % (10 min)
H	I	CH_3	**26**	53 s	81 % (10 min)	**33**	60 s	64 % (10 min)

from the plot of concentration (peak area at time t (A_t) divided by peak area at time zero (A_0) muliplied with 100 %) versus the irradiation time.

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