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(54) **CARBAMOYLATION OF AMINES, THIOPHENOLS, MERCAPTANES AND PHENOLS EMPLOYING ORGANIC AZIDES**

USPC ..... **564/32**; 560/132; 560/343; 562/27; 552/1; 568/61; 568/716

(75) Inventors: **Andrey Yagodkin**, Kuopio (FI); **Alex Azhayev**, Siilinjärvi (FI)

(58) **Field of Classification Search**  
USPC ..... 564/32; 560/343, 132; 562/27; 568/61, 568/716; 552/1  
See application file for complete search history.

(73) Assignee: **Metkinen Chemistry Oy**, Kuusisto (FI)

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CPC ..... **C07C 273/1827** (2013.01); **C07C 269/02** (2013.01); **C07C 333/02** (2013.01); **C07C 263/00** (2013.01); **C07C 247/00** (2013.01); **C07C 321/00** (2013.01); **C07C 39/00** (2013.01)

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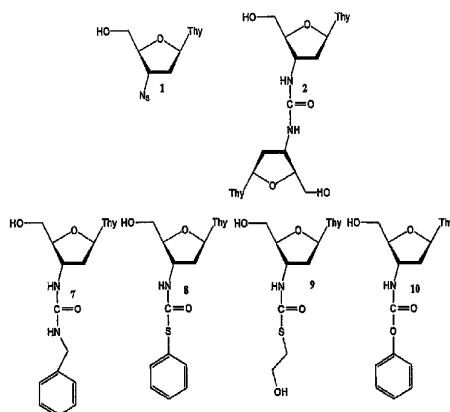
*Assistant Examiner* — Amy C Bonaparte

(74) *Attorney, Agent, or Firm* — Birch, Stewart, Kolasch & Birch, LLP

(57) **ABSTRACT**

The present invention relates to carbamoylation of amines, mercaptanes, thiophenols and phenols employing organic azides. More specifically, the invention relates to a method for generating urea derivatives, thiocarbamate derivatives and carbamate derivatives, and is based on the intermediate formation of isocyanate, starting from an organic azide. The reaction as described is useful in applications for modified nucleoside synthesis, oligonucleotide synthesis, as well as modification, labeling and conjugation of polymers and biomolecules.

**13 Claims, 4 Drawing Sheets**



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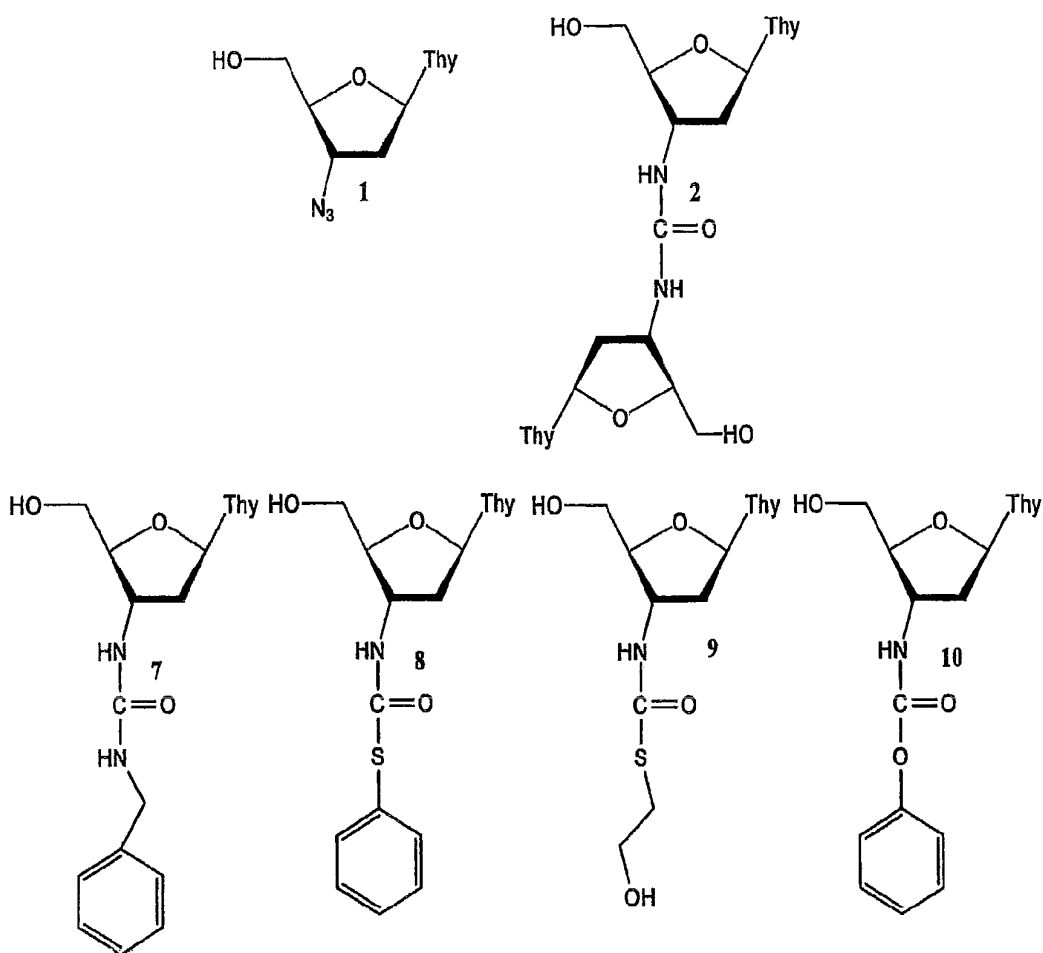


Figure 1

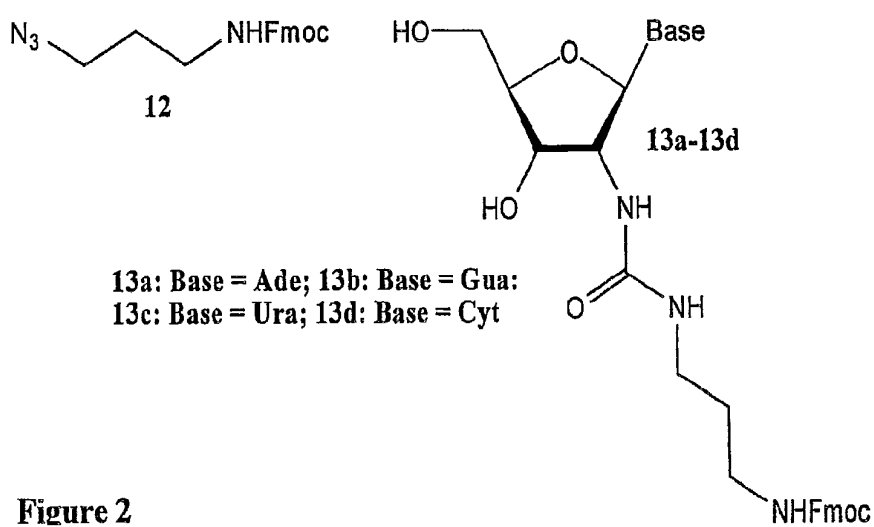


Figure 2

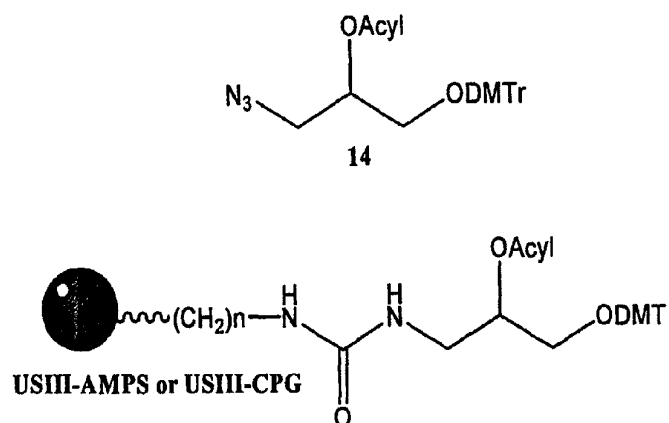


Figure 3

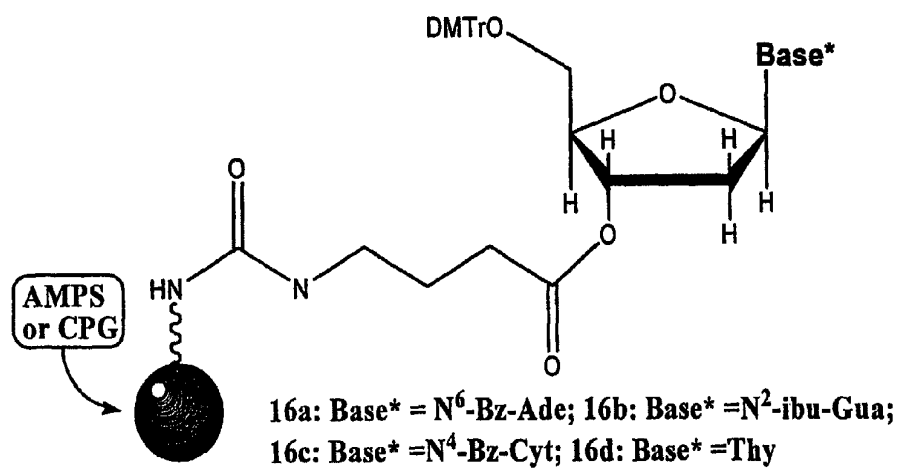


Figure 4

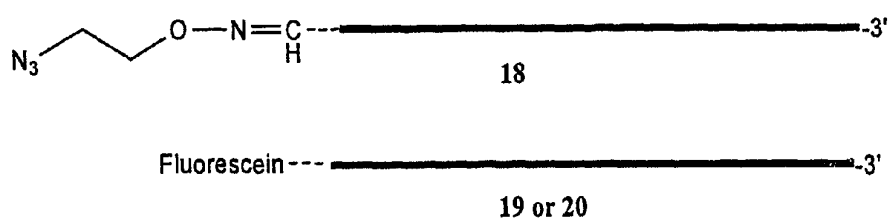


Figure 5

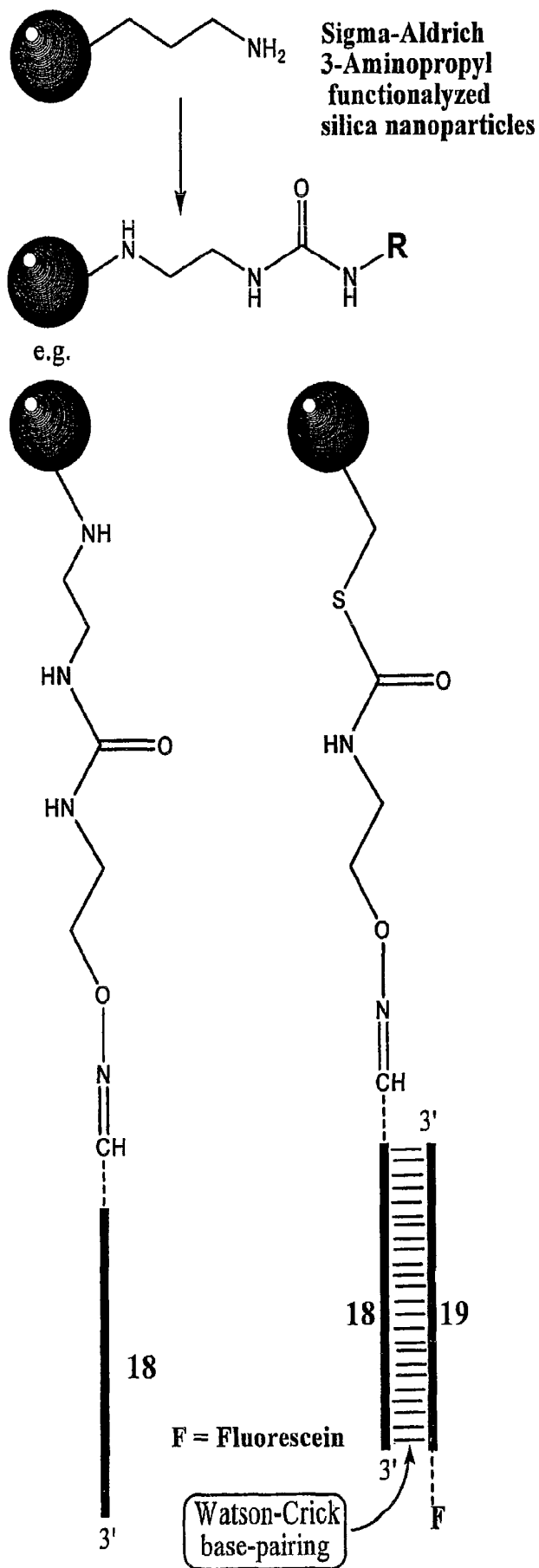


Figure 6

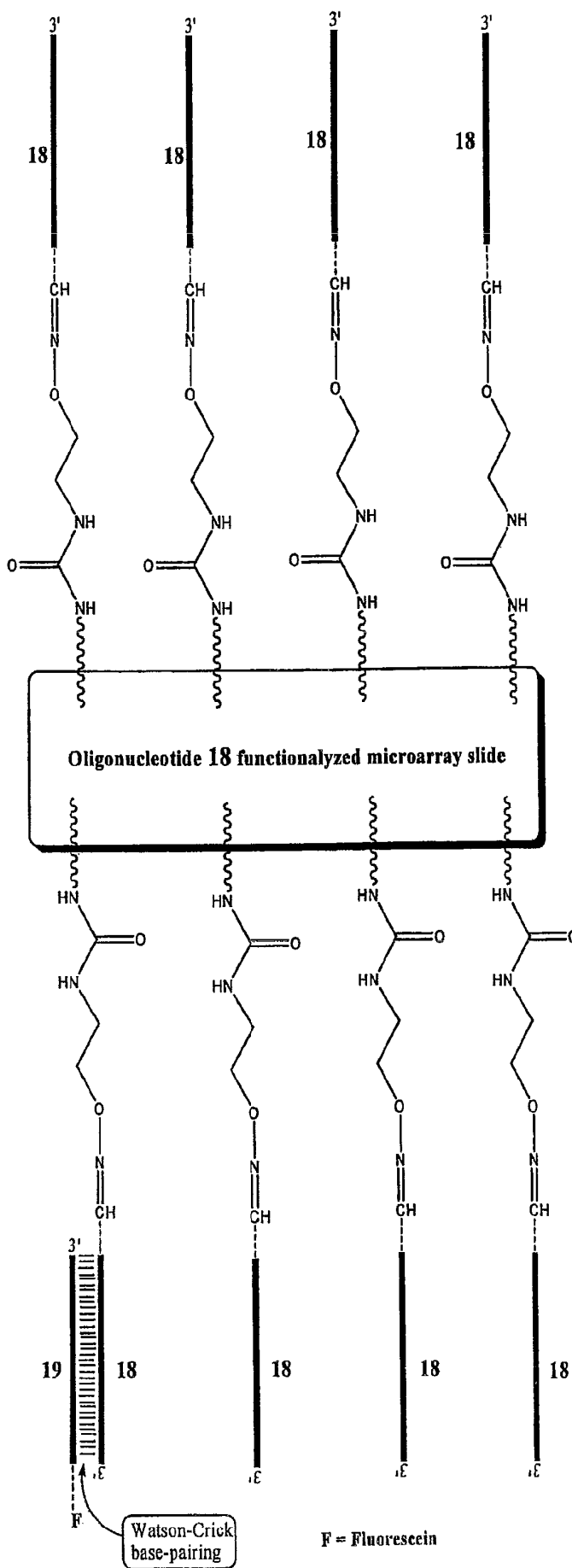


Figure 7

**CARBAMOYLATION OF AMINES,  
THIOPHENOLS, MERCAPTANES AND  
PHENOLS EMPLOYING ORGANIC AZIDES**

The present application is a national phase application filed under 35 U.S.C. §371 based on PCT/FI2007/050575 filed on Oct. 25, 2007. PCT/FI2007/050575 claims priority to U.S. Provisional Application No. 60/854,721 filed Oct. 27, 2006 and to Application No. 20075169 filed in Finland on Mar. 12, 2007 under 35 U.S.C. §119(a) and (e), the entire contents of the above-described applications are hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates to carbamylation of amines, mercaptanes, thiophenols and phenols employing organic azides. More specifically, the invention relates to a method for generating urea derivatives, thiocarbamate derivatives and carbamate derivatives, and is based on the intermediate formation of isocyanate, starting from an organic azide. The reaction as described is useful in applications for modified nucleoside synthesis, oligonucleotide synthesis, as well as modification, labeling and conjugation of polymers and biomolecules.

BACKGROUND OF THE INVENTION

International patent application No. WO 2005/061445 (Langstrom et al.) (1) and references cited therein are describing carbonylation via isocyanate using azides and carbon monoxide. This reaction is promoted by a transition metal complex (e.g. rhodium, palladium) and is performed in a high pressure reaction chamber. The main features of Langstrom's and similar methods are as follows: Introduction of carbon monoxide into the reaction chamber via the gas inlet and introduction at high pressure an azide solution mixed with a transition metal complex and a liquid reagent (solvent) into the reaction chamber via the liquid inlet. Since Langstrom method is dealing with carbon-isotope monoxide, additional technical measures have to be undertaken for trapping the carbon-isotope dioxide and converting it to carbon-isotope monoxide.

Obviously, these reactions require very special equipment, alkyl azide solution, expensive transition metal complex and hazardous highly toxic gas—carbon monoxide.

In contrast to this kind of procedure, the present method utilizes an alkyl azide solution, inexpensive compound of trivalent phosphorous (e.g. triphenylphosphine) and trialkylammonium hydrogen carbonate buffer. This buffer is prepared by simple bubbling of harmless carbon dioxide in a mixture of trialkylamine and water until pH about 7-8 is reached. The carbamylation reaction itself is then performed in a tightly closed vessel, like, e.g. a bottle with a screw cap.

It is noteworthy that the present procedure is extremely simple. It does not require any special equipment (unlike Langstrom's (1) or similar procedures), any expensive transition metal complexes or, more importantly, a hazardous highly toxic gas—carbon monoxide. In other words, the present procedure may be carried out in any chemical laboratory.

SUMMARY OF THE INVENTION

The present invention relates to a straightforward method of carbamylation of amines, mercaptanes, thiophenols and phenols, employing an organic azide, a compound of trivalent

phosphorous, an aqueous trialkylammonium hydrogen carbonate buffer and an organic solvent. This method may be successfully employed in basic organic chemistry, and also for the synthesis of various nucleoside derivatives and modification of various particles and solid surfaces.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 shows transformations of 3'-azido-3'-deoxythymidine.

FIG. 2 shows modification of 2'-amino-2'-deoxynucleosides.

FIG. 3 shows modification of polystyrene and/or controlled pore glass based solid supports resulting in Universal Solid Supports for oligonucleotide synthesis (6,7).

FIG. 4 shows modification of polystyrene and/or controlled pore glass based solid supports resulting in Nucleoside-bound solid supports for oligonucleotide synthesis (8).

FIG. 5 schematically shows azidoalkyl-tethered synthetic oligonucleotide for subsequent attachment to solid phases and surfaces and fluorescein-labeled synthetic oligonucleotides for testing oligonucleotide-derivatized nanoparticles and microarray slides.

FIG. 6 shows oligonucleotide-functionalized nanoparticles.

FIG. 7 shows an oligonucleotide-functionalized microarray slide.

DETAILED DESCRIPTION OF THE INVENTION

Abbreviations

Ade Adenin-9-yl  
AMPS Macroporous Aminomethyl Polystyrene  
CPG Controlled Pore Glass  
Cyt Cytosin-1-yl  
DMTr 4,4'-Dimethoxytriphenylmethyl  
Gua Guanin-9-yl  
Fmoc 9-Fluorenylmethoxycarbonyl  
N<sup>6</sup>-Bz-Ade N<sup>6</sup>-Benzoyl-Adenin-9-yl  
N<sup>4</sup>-Bz-Cyt N<sup>4</sup>-Benzoyl-Cytosin-1-yl  
N<sup>2</sup>-ibu-Gua N<sup>2</sup>-isobutyryl-Guanin-9-yl  
Thy Thymin-1-yl  
Ura Uracil-1-yl  
USIII Universal Solid Support III

The present invention relates to the reaction of carbamylation of amines Ia, mercaptanes Ib, thiophenols Ic or phenols Id, employing organic azides II (Scheme 1). The reaction proceeds via intermediate formation of isocyanates of general formulae III and results in products of general formulae IV.

Basic chemistry of various transformations mentioned herein is depicted as follows from Scheme 2.

The organic group R in Schemes 1 and 2 may be any organic group capable of forming an organic azide compound. Consequently, R may be linear or cyclic lower alkyl, which may optionally be substituted, arylalkyl, aminoalkyl, or lower alcohol. R may also be nucleosidyl, nucleotidyl, oligonucleotidyl or peptidyl, as well as ribosyl, 2'-deoxyribosyl or any functional derivative thereof. In any of the mentioned organic groups any functional group may be protected, if appropriate. Preferably R is lower aminoalkyl or nucleosidyl, more preferably 3-aminopropyl or 3'-deoxythymidyl.

R' as an aliphatic organic group is preferably linear or cyclic lower alkyl, which is optionally substituted, or deoxynucleosidyl. R' is in this case, for instance, hydroxyethyl.

R' as an aromatic organic group is preferably aryl or substituted aryl. R' is in this case, for instance, phenyl or benzyl.

The method of synthesis described in the present application comprises reduction of organic azides II with a compound of trivalent phosphorous (triphenylphosphine, trialkylphosphine, trialkylphosphite, hexaalkyltriamidophosphite, etc.) in an organic solvent (1,4-dioxane, tetrahydrofurane, acetonitrile, etc.) in the presence of hydrogen carbonate ions (various trialkylammonium hydrogen carbonate buffers, e.g. trimethylammonium hydrogen carbonate, triethylammonium hydrogen carbonate, diethyl-2-hydroxyethylammonium hydrogen carbonate, etc.), leading to formation of intermediate structures incorporating  $\text{—P=N—}$  function, followed by formation of isocyanates III and finally by reaction with amines, mercaptanes, thiophenols or phenols as nucleophiles to give rise to ureas IVa, thiocarbamates IVb and IVc or carbamates IVd.

The procedure to generate substituted ureas IVa, thiocarbamates IVb,c and carbamates IVd is the preferred method of the present invention by virtue of its broad employment for synthesis and modification of various organic compounds.

Since the intermediate reactive product of this reaction is an isocyanate of structure III, the present invention may be successfully utilized in chemical synthesis and chemical industry, where generation of isocyanates is required or where isocyanates serve as starting compounds. The present invention discloses a procedure which complements a number of contemporary methods of synthesis and manufacture of isocyanates (2, 3, 4, 5).

The procedure is a highly effective and simple new conjugation reaction that is complementing conventional methods of bioconjugation. It is applicable in diverse areas including applications for oligonucleotide synthesis, modification and conjugation. More broadly it may find use in nanotechnology, arrays, diagnostics and screening assays. The technique can be readily engineered to link small molecules (peptides, fluorophores, oligonucleotides, etc.), biomolecules (proteins, DNA, RNA, antibodies), or other molecules to solid surfaces (beads, glass, plastic, latex), for applications in proteomics, genomics, drug discovery, diagnostics and therapeutics. The present invention will also enable the development of new applications in both genomics and proteomics that cannot be satisfied with current conventional methods.

Advantages of the present technology include:

- simple and easy-to-use protocol;
- carrying out the reactions at room temperature in an organic solvent containing aqueous buffered media and yielding a high-efficiency conjugation;
- obtaining conjugates which have extended stability.

Consequently, the present invention may be utilized in processes in which generation of isocyanates is required or where isocyanates serve as starting compounds to react with aminoalkyl, mercaptoalkyl, thiophenylalkyl and hydroxyphenylalkyl functions.

In more detail, the present invention allows to generate the above-mentioned structures as bridges for:

- conjugation of molecules bearing azidoalkyl tethers with molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups;
- conjugation of molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with molecules bearing azidoalkyl groups;
- conjugation of nucleosides, nucleotides and oligonucleotides bearing azidoalkyl tethers with various molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups (luminescent and spin labels, various chelates, modified peptides, modified proteins, modified antibodies, etc.);

conjugation of nucleosides, nucleotides and oligonucleotides bearing azidoalkyl tethers with peptides, proteins, antibodies, etc.;

conjugation of molecules (luminescent and spin labels, various chelates, etc.) bearing azidoalkyl tethers with peptides, proteins, antibodies, etc.;

conjugation of nucleosides, nucleotides and oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with various molecules bearing azidoalkyl groups (luminescent and spin labels, various chelates, modified peptides, modified proteins, modified antibodies, etc.);

conjugation of oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with solid phase bearing azidoalkyl groups to prepare oligonucleotide arrays, oligonucleotide-bound microparticles, nanoparticles, etc.;

conjugation of oligonucleotides bearing azidoalkyl tethers with solid phase bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl and hydroxyphenylalkyl groups to prepare oligonucleotide arrays, oligonucleotide-bound microparticles, nanoparticles, etc.;

conjugation of protected nucleosides bearing azidoalkyl tethers with various solid matrices (controlled pore glass, polystyrene, polyvinylacetate) bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups to prepare nucleoside-bound solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of protected nucleosides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl and hydroxyphenylalkyl tethers with various solid matrices (controlled pore glass, polystyrene, polyvinylacetate) bearing azidoalkyl groups to prepare nucleoside-bound solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of specific molecules bearing azidoalkyl tethers with various solid matrices (controlled pore glass, polystyrene, polyvinylacetate) bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl and hydroxyphenylalkyl groups to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of specific molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl and hydroxyphenylalkyl tethers with various solid matrices (controlled pore glass, polystyrene, polyvinylacetate), bearing azidoalkyl groups to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis.

## EXAMPLES

### 1. 3'-Azido-3'-deoxythymidine derivatives

#### Example 1

3'-Azido-3'-deoxythymidine (1, 0.37 mmol) was added to a solution of triphenylphosphine (0.4 mmol) in a mixture of dioxane (4 ml) and 1M aqueous triethylammonium hydrogen carbonate (0.5 ml). The mixture was left for 24 hours at room temperature and evaporated to dryness. Chromatographic separation on silica gel afforded dimer 2 (FIG. 1) in 53% yield.



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## Example 2

3'-Azido-3'-deoxythymidine (1, 0.37 mmol) was added to a solution of 1 mmol of compound benzylamine (3) or thiophenol (4) or mercaptoethanol (5) or phenol (6) and triphenylphosphine (0.4 mmol) in a mixture of dioxane (4 ml) and 1M aqueous triethylammonium hydrogen carbonate (0.5 ml). The mixture was left for 4 hours (for compounds 7-9) or for 24 hours (for compound 10) at room temperature and evaporated to dryness. Chromatographic separation on silica gel afforded compounds 7-9 in about 90% yield; compound 10 in 5% yield (FIG. 1).

## Example 3

3'-Azido-3'-deoxythymidine (1, 0.37 mmol) was added to a solution of 1 mmol of compound benzylamine (3) and 1 mmol of mercaptoethanol (5) and triphenylphosphine (0.4 mmol) in a mixture of dioxane (4 ml) and 1M aqueous triethylammonium hydrogen carbonate (0.5 ml). The mixture was left for 12 hours at room temperature and analyzed with RP HPLC. The HPLC trace and integration of peaks revealed the complete conversion of azide 1 to give compounds 7 and 9 in 2:1 ratio (FIG. 1).

## 2. Modification of Aminonucleosides

## Example 4

2'-Amino-2'-deoxynucleoside (11a-d, 0.37 mmol) was added to a solution of 1 mmol of azide 12 and triphenylphosphine (0.4 mmol) in a mixture of dioxane (4 ml) and 1M aqueous triethylammonium hydrogen carbonate (0.5 ml). The mixture was left for 24 hours at room temperature and evaporated to dryness. Chromatographic separation on silica gel afforded compounds 13a-d in about 80% yield (FIG. 2).

## 3. Modification of Particles and Solid Surfaces

## A. Modification of Polystyrene and Controlled Pore Glass Based Solid Supports Resulting in Universal Solid Supports for Oligonucleotide Synthesis (6,7)

## Example 5

A solution of azide 14 in dioxane (11.5 ml of 0.09 M solution for 0.4 mmol of linker loaded support; 23 ml of 0.09 M solution for 0.8 mmol of linker loaded support) was added to a suspension of 20 g of Macroporous Aminomethyl polystyrene (cross-linking—60%, particle size—100-200 mesh, loading of amino groups—0.12 mmol/g) in dioxane (188 ml for 0.4 mmol of linker loaded support; 177 ml for 0.8 mmol of linker loaded support). To the resulting suspension the aqueous solution of triethylammonium hydrogen carbonate (2 M, 5 ml) and triphenylphosphine (3 g for 0.4 mmol of linker loaded support; 6 g for 0.8 mmol of linker loaded support) were added and the mixture was shaken for 48 h at room temperature. The resin was filtered off, washed with acetone, followed by tetrahydrofuran and re-suspended in tetrahydrofuran (50 ml). A mixture of pyridine (70 ml) and acetic anhydride (30 ml) was then added and the resulting suspension was left for 3 h at room temperature with periodic shaking. The resin was filtered off, washed with pyridine (30 ml), acetone (200 ml), 0.1% triethylamine in ether and finally dried in high vacuum. The resulting dry resin, contained

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either about 0.04 mmol of DMTr-groups per gram of polymer (8)—(USIII-AMPS-40) (FIG. 3), or about 0.08 mmol of DMTr-groups per gram of polymer (8)—(USIII-AMPS-80) (FIG. 3). Both polymers, Universal Solid Supports for Oligonucleotide synthesis (USIII-AMPS-40 and USIII-AMPS-80), performed identically to the Universal Solid Support, described in detail earlier (6,7).

## Example 6

A solution of azide 14 in dioxane (11.5 ml of 0.09 M solution) was added to a suspension of 20 g of Aminoalkyl Controlled Pore Glass (CPG-500: particle size—120-200 mesh, loading of amino groups—0.12 mmol/g, pore diameter 500 Å or CPG-1000: particle size—120-200 mesh, loading of amino groups—0.06-0.07 mmol/g, pore diameter 1000 Å) in dioxane (188 ml). To the resulting suspension the aqueous solution of triethylammonium hydrogen carbonate (2 M, 5 ml) and triphenylphosphine (3 g) were added and the mixture was shaken for 48 h at room temperature. The resin was filtered off, washed with acetone, followed by tetrahydrofuran and re-suspended in tetrahydrofuran (50 ml). A mixture of pyridine (70 ml) and acetic anhydride (30 ml) was then added and the resulting suspension was left for 3 h at room temperature with periodic shaking. The solid phase was filtered off, washed with pyridine (30 ml), acetone (200 ml), 0.1% triethylamine in ether and finally dried in high vacuum. The resulting dry solid phase contained: about 0.04 mmol of DMTr-groups per gram of CPG-500 (8)—USIII-CPG-500-40 (FIG. 3), or about 0.03 mmol of DMTr-groups per gram of CPG-1000 (8)—USIII-CPG-1000-30 (FIG. 3). Both solid phases, Universal Solid Supports for Oligonucleotide synthesis (USIII-CPG-500-40 and USIII-CPG-1000-30), performed identically to the Universal Solid Support, described in detail earlier (6,7).

## Example 7

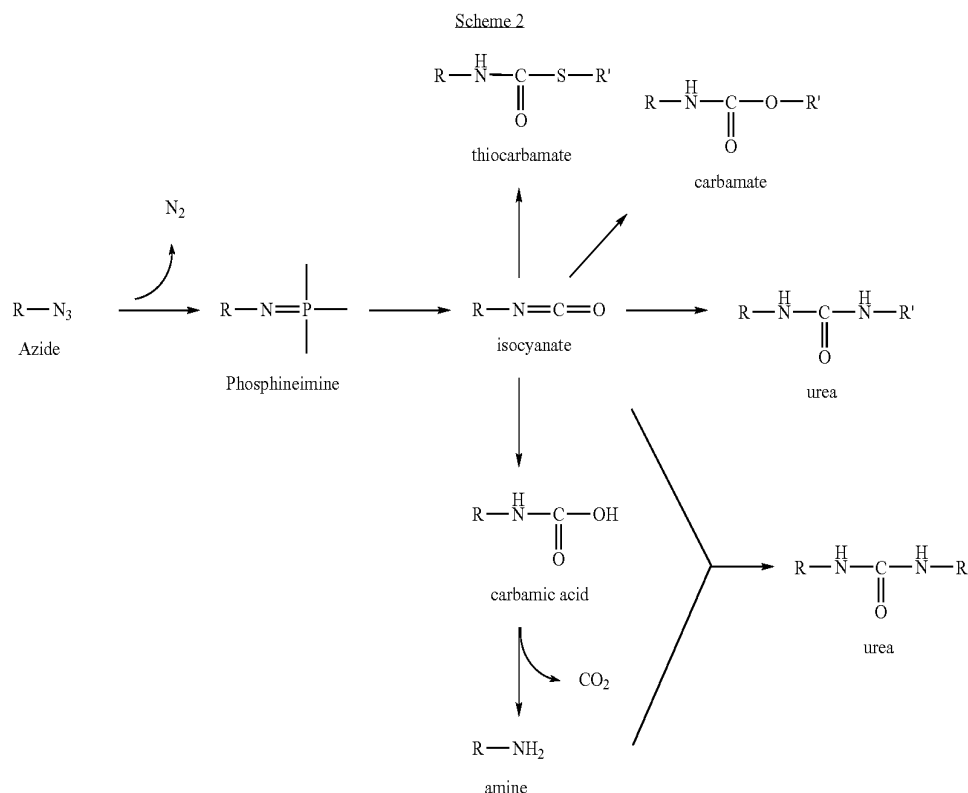
Aminoalkyl Controlled Pore Glass (CPG-500: particle size—120-200 mesh, loading of amino groups—0.12 mmol/g, pore diameter 500 Å or CPG-1000: particle size—120-200 mesh, loading of amino groups—0.06-0.07 mmol/g, pore diameter 1000 Å) or Macroporous Aminomethyl polystyrene (cross-linking—60%, particle size—100-200 mesh, loading of amino groups—0.12 mmol/g) were derivatized with 3'-O-(4-azidobutyryl)-5'-O-dimethoxytrityl-N-acyl-nucleosides 16a or 16b or 16c or 3'-O-(4-azidobutyryl)-5'-O-dimethoxytritylthymidine 16d. Procedures for derivatization were described in Examples 4-6. The resulting dry solid phases contained 0.03-0.08 mmol of DMTr-groups per gram of solid support (8). All four nucleoside-bound solid supports 17a-d (FIG. 4) performed well in standard oligonucleotide synthesis.

## B. Derivatization of Nanoparticles with Oligonucleotide

## Example 8

Sigma-Aldrich 3-Aminopropyl-functionalized silica nanoparticles, 3% (w/v) in ethanol (average particle size=15 nm), 2.5 ml were evaporated to dryness and re-suspended in dioxane (1.9 ml).





The invention claimed is:

1. A method for the preparation of a compound of formula IV



wherein

—R is an aliphatic or aromatic organic group, and R' is an aliphatic organic group and X is NH; S or NR", wherein R" is alkyl; or

R' is an aromatic organic group and X is S or O, comprising

(a) reacting a compound of formula  $\text{R}-\text{N}_3$  (II), wherein R is as defined above, with a compound of trivalent phosphorous in the presence of an aqueous solution of hydrogen carbonate ions, in an organic solvent, to obtain an isocyanate of formula III



wherein R is as defined above, and

(b) reacting the isocyanate of formula III with a compound of formula  $\text{R}'-\text{XH}$ , wherein R' and X are as defined above,

to obtain a compound of formula IV.

2. The method according to claim 1, wherein R as an organic group is a group capable of forming an organic azido compound.

3. The method according to claim 2, wherein R is linear or cyclic lower alkyl, which may optionally be substituted, arylalkyl, aminoalkyl, lower alcohol, nucleosidyl, nucleotidyl, oligonucleotidyl, peptidyl, ribosyl or T-deoxyribosyl, in which any functional group may be protected.

4. The method according to claim 1, wherein R' as the aliphatic organic group is linear or cyclic lower alkyl, which is optionally substituted, or deoxynucleosidyl.

5. The method according to claim 1, wherein R' as the aromatic organic group is aryl or substituted aryl.

6. The method according to claim 1, wherein the compound of trivalent phosphorous is selected from the group consisting of triphenylphosphine, trialkylphosphine, trialkylphosphite and hexaalkyltriamidophospite.

7. The method according to 1, wherein the organic solvent is selected from the group consisting of 1,4-dioxane, tetrahydrofuran and acetonitrile.

8. The method according to claim 1, wherein the hydrogen carbonate ions are provided by an aqueous trialkylammonium hydrogen carbonate buffer.

9. The method according to claim 8, wherein the trialkylammonium hydrogen carbonate is selected from the group consisting of trimethylammonium hydrogen carbonate, triethylammonium hydrogen carbonate and diethyl-2-hydroxyethylammonium hydrogen carbonate.

10. The method according to claim 1 wherein X is NH or NR", for the preparation of urea derivatives.

11. The method according to claim 1 wherein X is S, for the preparation of thiocarbamate derivatives.

12. The method according to claim 1 wherein X is O, for the preparation of carbamate derivatives.

13. The method according to claim 1 for conjugation of molecules bearing azidoalkyl tethers with molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups;

conjugation of molecules bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with molecules bearing azidoalkyl groups;

conjugation of nucleosides, nucleotides and oligonucleotides bearing azidoalkyl tethers with luminescent and spin labels, various chelates, modified proteins and modified antibodies bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups;

conjugation of nucleosides, nucleotides and oligonucleotides bearing azidoalkyl tethers with peptides, proteins or antibodies;

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conjugation of luminescent and spin labels and various chelates bearing azidoalkyl tethers with peptides, proteins or antibodies;

conjugation of nucleosides, nucleotides and oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with luminescent and spin labels, various chelates, modified peptides, modified proteins and modified antibodies bearing azidoalkyl groups;

conjugation of protected nucleosides bearing azidoalkyl tethers with solid matrices of controlled pore glass, polystyrene or polyvinylacetate bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups, to prepare nucleoside-bound solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of protected nucleosides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with solid matrices of controlled pore glass, polystyrene or polyvinylacetate bearing azidoalkyl groups, to prepare nucleoside-bound solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of oligonucleotides bearing azidoalkyl tethers with various solid matrices, including controlled pore glass, polystyrene and polyvinylacetate, bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with controlled pore glass, polystyrene and polyvinylacetate solid matrices bearing azidoalkyl groups, to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of oligonucleotides bearing azidoalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides, derivatized with aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups;

conjugation of oligonucleotides bearing azidoalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides, derivatized with aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups, to prepare oligonucleotide arrays, oligonucleotide bound microparticles or nanoparticles;

conjugation of oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides bearing azidoalkyl groups, to prepare oligonucleotide arrays, oligonucleotide-bound microparticles or nanoparticles.

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nylalkyl groups to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with controlled pore glass, polystyrene and polyvinylacetate solid matrices bearing azidoalkyl groups, to prepare universal solid supports for DNA, RNA and modified oligonucleotide solid phase synthesis;

conjugation of oligonucleotides bearing azidoalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides, derivatized with aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups;

conjugation of oligonucleotides bearing azidoalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides, derivatized with aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl groups, to prepare oligonucleotide arrays, oligonucleotide bound microparticles or nanoparticles;

conjugation of oligonucleotides bearing aminoalkyl, mercaptoalkyl, thiophenylalkyl or hydroxyphenylalkyl tethers with solid matrices of silica gel, polystyrene, polyvinylacetate, micro- and nanoparticles and microarray slides bearing azidoalkyl groups, to prepare oligonucleotide arrays, oligonucleotide-bound microparticles or nanoparticles.

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