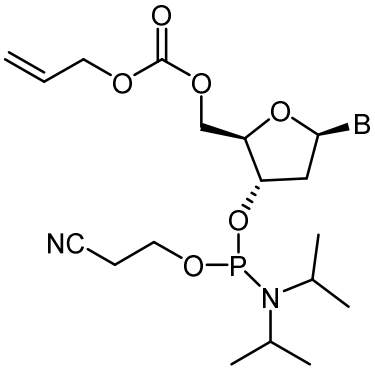
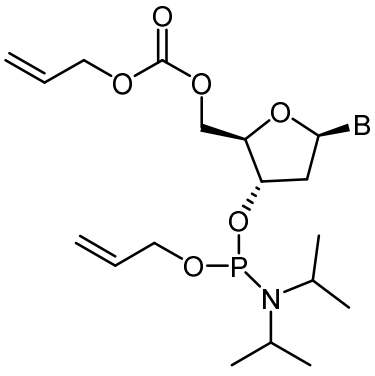
- B is a monocyclic or bicyclic C_{4-6} heterocyclic ring. Further provided herein are methods wherein R^1 is straight chain alkenylene. Further provided herein are methods wherein R^1 is straight chain C_{2-6}alkenylene. Further provided herein are methods wherein R^1 is allyl. Further provided herein are methods wherein R^1 is branched chain alkenylene. Further provided herein are methods wherein R^1 is branched chain C_{3-8}alkenylene. Further provided herein are methods wherein R^2 is substituted alkylene. Further provided herein are methods wherein R^2 is substituted C_{2-4}alkylene. Further provided herein are methods wherein R^2 is cyanoethyl. Further provided herein are methods wherein R^2 is unsubstituted alkenylene. Further provided herein are methods wherein R^2 is unsubstituted C_{2-4}alkylene. Further provided herein are methods wherein R^2 is allyl. Further provided herein are methods wherein B is a monocyclic C_4 heterocyclic ring. Further provided herein are methods wherein B is a bicyclic C_5 heterocyclic ring. Further provided herein are methods wherein B is a nucleobase. Further provided herein are methods wherein at least three of R^3, R^4, R^5, R^6, R^7, R^8, and R^9 are H. Further provided herein are methods wherein R^3 is H and R^4 is OH. Further provided herein are methods wherein one or both of R^3 and R^4 is F. Further provided herein are methods wherein one or both of R^3 and R^4 is $-OCH_3$ or $-OCH_2CH_2OCH_3$. Further provided herein are methods wherein the protected nucleoside has the structure:



. Further provided herein are methods wherein the protected nucleoside has the structure:



.

[0004a] In one aspect, there is provided a method of synthesizing a polynucleotide comprising: coupling at least one nucleoside attached to a solid support to a protected nucleoside, wherein the protected nucleoside comprises a protecting group, wherein the protecting group comprises a branched alkenylene, wherein the solid support comprises an addressable array; and wherein the

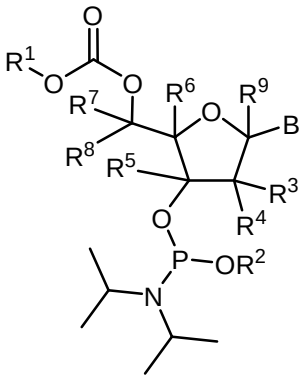
addressable array comprises a plurality of loci; contacting an amount of a reagent with the protected nucleoside, wherein the contacting results in deprotection of the protected nucleoside; and repeating the coupling and contacting steps to synthesize the polynucleotide.

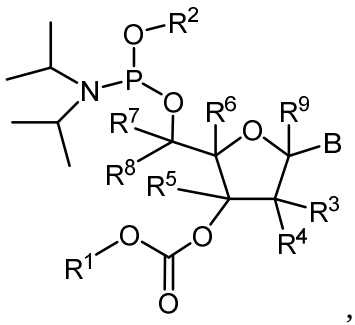
[0005] Provided herein are devices configured to perform the methods described herein. Further provided herein are devices wherein the addressable array comprises at least 1000 addressable loci for synthesis. Further provided herein are devices wherein the addressable array comprises a pitch distance of 10-200 nm.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of synthesizing a polynucleotide comprising:
   coupling at least one nucleoside attached to a solid support to a protected nucleoside, wherein the protected nucleoside comprises a protecting group, wherein the protecting group comprises a branched alkenylene, wherein the solid support comprises an addressable array; and wherein the addressable array comprises a plurality of loci;
   contacting an amount of a reagent with the protected nucleoside, wherein the contacting results in deprotection of the protected nucleoside; and
   repeating the coupling and contacting steps to synthesize the polynucleotide.
2. The method of claim 1, wherein the amount of the reagent is less than about 15 mol% of the protected nucleoside.
3. The method of claim 1 or 2, wherein the protecting group protects a 5' hydroxyl of the protected nucleoside.
4. The method of any one of claims 1-3, wherein the reagent comprises a transition metal catalyst.
5. The method of claim 4, wherein the transition metal catalyst comprises:
   a zero oxidation state;
   a Pd(0) catalyst;
   one or more phosphine ligands; and/or
   $Pd(Ph_3)_4$.
6. The method of any one of claims 1-5, further comprising contacting the protected nucleoside with a nucleophile.
7. The method of any one of claims 1-6, wherein the reagent is in contact with the protected nucleoside for less than about 10 minutes.
8. The method of any one of claims 1-7, wherein the method further comprises capping, wherein capping comprises applying acetyl chloride or acetic anhydride to the solid support.
9. The method of any one of claims 1-8, wherein the polynucleotide is 50-300 bases in length.
10. The method of any one of claims 1-9, further comprising applying a voltage to a solvent in fluid communication with the protected polynucleotide, wherein the voltage is applied for a duration of 0.1 seconds to 10 seconds.
11. The method of any one of claims 1-10, wherein the protected nucleoside comprises the formula:



or


,

wherein:

R^1 is a branched alkenylene;

R^2 is alkylene or alkenylene, each of which is independently unsubstituted or substituted;

each R^3, R^4, R^5, R^6, R^7, R^8, or R^9 is independently H, OH, a halogen, an O-alkyl, an N-alkyl, an O-alkyl-O-alkyl, an azide, or

R^3 and R^6 are taken together to form a ring; and

B is a monocyclic or bicyclic $C_{4\text{-}6}$ heterocyclic ring.

12. The method of claim 11, wherein one or both of R^3 and R^4 is:

F;

OCH_3; or

$OCH_2CH_2OCH_3$.

13. The method of claim 1, wherein the reagent comprises a Pd(0) complex with negatively charged aryl-sulfonate containing phosphine ligands.

14. The method of claim 13, further comprising:

applying a voltage to one or more loci to electrophoretically attract the Pd(0) complex with negatively charged phosphine ligands to selected loci to deprotect the protected nucleoside.

15. The method of claim 1, wherein each polynucleotide of the plurality of polynucleotides synthesized has a different sequence from another polynucleotide of the plurality of polynucleotides.

16. The method of claim 1, further comprising:

selectively reducing a Pd(II) precursor at one or more loci of the addressable array to generate a Pd(0) catalyst;

contacting the protected nucleoside with the Pd(0) catalyst and a nucleophile to deprotect the protected nucleoside.

17. The method of claim 1, wherein the plurality of polynucleotides are synthesized at a rate of about 100 nucleotides per hour.

18. The method of claim 6, wherein the nucleophile is N,N-dimethylbarbiturate.

19. The method of claim 1, further comprising an oxidation step, wherein the oxidation step comprises treatment with iodine, water, and a base, wherein the base is selected from pyridine, lutidine, or collidine.

20. The method of claim 1, wherein the protecting group comprising a branched alkenylene is protecting a 3’ hydroxyl of the protected nucleoside.