Accepted Manuscript

An efficient method to synthesize novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides

A-Peng Wang, Chao Liu, Shuang Yang, Zhehui Zhao, Pingsheng Lei

PII: S0040-4020(15)30214-3

DOI: 10.1016/j.tet.2015.11.029

Reference: TET 27286

To appear in: *Tetrahedron*

Received Date: 8 September 2015

Revised Date: 7 November 2015

Accepted Date: 16 November 2015

Please cite this article as: Wang A-P, Liu C, Yang S, Zhao Z, Lei P, An efficient method to synthesize novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.11.029.

Graphical Abstract

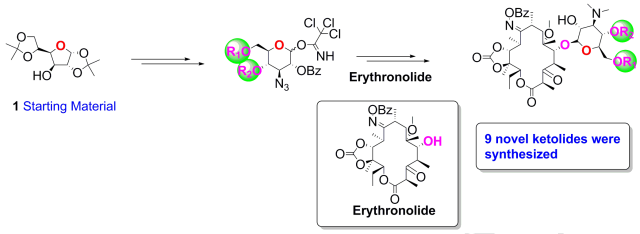
To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

An efficient method to synthesize novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides

A-Peng Wang, Chao Liu, Shuang Yang, Zhehui Zhao*, Pingsheng Lei*

State Key Laboratory of Bioactive Substance and Function of National Medicines, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100050, PR China

Leave this area blank for abstract info.



Tetrahedron
journal homepage: www.elsevier.com

An efficient method to synthesize novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides

A-Peng Wang, Chao Liu, Shuang Yang, Zhehui Zhao*, Pingsheng Lei*

State Key Laboratory of Bioactive Substance and Function of National Medicines, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100050, PR China

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

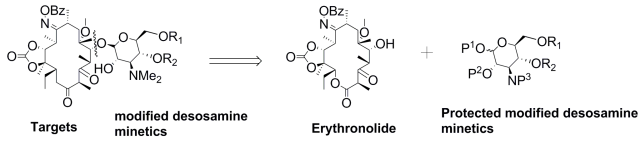
Keywords:
Ketolides
desosamine mimetics
mycaminose
glycosylation
modification

ABSTRACT

A new and facile procedure was developed to synthesize novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides by adopting different protective strategies and comparing various glycosylation conditions. Seven trichloroacetimidate donors which had different types of substituent groups at C-6 position were synthesized to couple with the erythronolide. Nine novel 5-*O*-(6′-modified)-mycaminose 14-membered ketolides were obtained to verify the utility of the method.

1. Introduction

5-*O*-desosamine of macrolide antibiotics is the most important pharmacophore which provides the major binding energy with the target bacterial ribosome.[1] Direct modification of 5-*O*-desosamine was focused on 2′-OH group and 3′- NMe_2 group which showed no activities or weak activities.[2] Modification of other positions was rarely reported due to the complexity of the macrolide structure and synthetic difficulty.[3] A strategy about the study of other positions of 5-*O*-desosamine was to synthesize new desosamine-mimetics to replace the desosamine. A series of 5-*O*-(4′-modified)-desosamine 14-membered ketolides were synthesized in our lab, in which 5-*O*-mycaminose ketolide showed obviously improved activity against certain sensitive pathogens compared to Clarithromycin.[4] For 6′-modified desosamine ketolide, the study on its synthesis and SARs was hardly reported previously. Liang et al had synthesized several different 5-*O*-desosamine modified ketolides, in which 5-*O*-(6′-OBz)-desosamine ketolide showed excellent activity against several erythromycin-resistant pathogens. However, only benzoyl group was studied for C-6 of desosamine. The method for C-6 modified desosamine and 5-*O*-(6′-modified)-desosamine ketolide was not published in detail.[5,6] It would be meaningful to develop this synthetic method to study the 5-*O*-(6′-modified)-desosamine ketolides further. Herein we reported a facile procedure of modifying C-6 of desosamine-mimetics and synthesizing a series of novel 5-*O*-(6′-modified)-desosamine-mimetics 14-membered ketolides which would provide an opportunity for the design of a new class of ketolides .

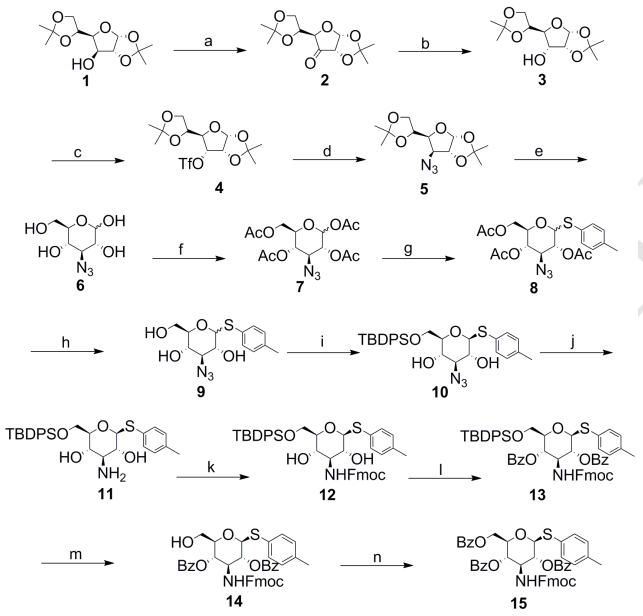


Scheme 1. Retrosynthesis of Targets

2. Results and discussion

The retrosynthetic analysis (Scheme 1) of targets adopted the strategy of replacement 5-*O*-desosamine with a modified desosamine mimetic. Erythronolide was obtained via 9 steps from Clarithromycin as the way Y, Xu et al reported in our lab.[4] 6-modified desosamine-mimetics were needed to be synthesized to couple with erythronolide. 5-*O*-(6′-modified)-desosamine ketolide was reported by Liang et al. [5,6] 4-Methylphenyl-thio glycosides were used as the donors in glycosidation and 3′-NMe_2 group was converted from 3′-NHFmoc group. The neighboring group participation effect of 2-OBz group in the donors determined the glycosylation product of β-configuration. Based on that, the synthetic route for compound **15** was designed (Scheme 2). Commercial available compound **1** was chosen as the starting material, compound **3** was obtained by two consecutive steps in a yield of 80% through oxidation with Dess - Martin periodinane and then reduction with $NaBH_4$.[7] Conversion of 3-OH group to 3-OTf group with Tf_2O formed compound **4** in 95% yield. 3-OTf group was a good leaving group which could be replaced by azide group to form compound **5** in 99% yield, 3-N_3 group was vital to be converted into 3-NH_2 group and 3-

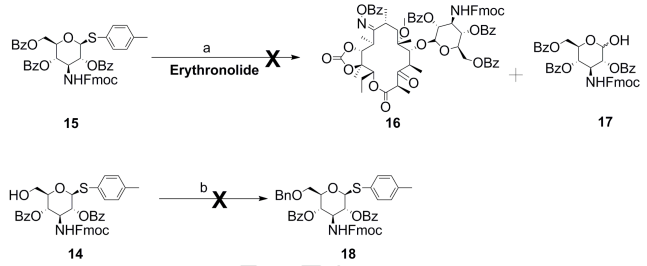
NHFmoc group.[8,9] After that, opening the five-memberd furan cyclic compound **5** with TFA and acylation with Ac_2O formed compound **7**, the yield of two steps was 80%.[10] The 1-OAc group could selectively react with 4-methylthiophenol to produce compound **8** in a yield of 87%.[11] 4-Methylphenyl-thio glycoside could not only be used as the glucosinolate but also be transformed to trichloroacetimidate. Adding MeONa to compound **8** in MeOH produced compound **9** in 95% yield.[12] By using TBDPSCl, 6-OH group could be selectively protected compared to 2-OH group and 4-OH group, the different protected groups assigned for the primary alcohol and secondary alcohol made the modification of C-6 possible. 6-OH group was selectively protected with TBDPSCl in pyridine to form compound **10** in a yield of 92%. Staudinger reduction of 3-N_3 group formed compound **11** in 80% yield.[13] After that, protection of 3-NH_2 group with FmocCl in the mixture of CH_2Cl_2 and $NaHCO_3$ aqueous solution produced compound **12** in 78% yield. Then, protection of 2-OH group and 4-OH group with BzCl yielded compound **13**. This manipulation was adopted based on that 3-N_3 group was hard to reduce under the existent of 2- and 4-*O*-benzoyl groups.[14] 6-OTBDPS group was selectively removed by adding hydrochloric acid to compound **13** in MeOH to form compound **14** in a yield of 79%.[15] The 6-OH group of compound **14** could be modified with suitable substituents. Compound **15** was synthesized ~~with BzCl~~ via 14 steps in a total yield of 15%.



Scheme 2. Reagents and conditions: a) Dess-Martin, CH_2Cl_2; b) $NaBH_4$, EtOH, ice-Bath, two steps, 80%; c) Tf_2O, pyridine, 95%; d) NaN_3, DMF, 99%; e) TFA, H_2O; f) Ac_2O, pyridine, two steps, 80%; g) 4-methylthiophenol, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 87%; h) MeONa, MeOH, 95%. i) TBDPSCl, DMAP, pyridine, 92%; j) PhP_3, THF, H_2O, 80%; k) FmocCl, aq. $NaHCO_3$, CH_2Cl_2, 78%; l) BzCl, pyridine, 81%; m) HCl, MeOH, 79%; n) BzCl, pyridine, 80%.

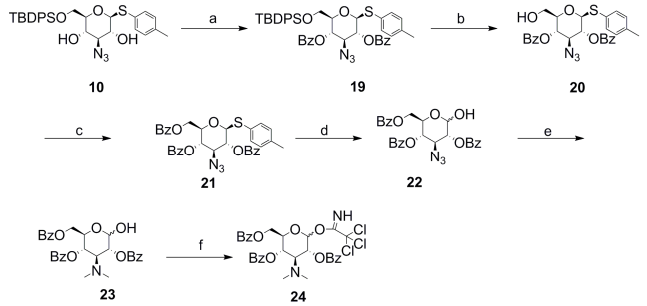
With the donor **15** in hand, the acceptor erythronolide and donor **15** were coupled using NIS and AgOTf in dry CH_2Cl_2 at -78 ℃. However, the glycosidation failed even though the reaction time was prolonged to 24 hours. Glycosylation product **16** was not found (Scheme **3**). By using different reaction conditions such as adjustment of reaction temperature and / or reactants ratio, the desired product **16** was not found. According to the work Y, Xu et al reported,[4] the 5-OH of erythronolide showed low reactivity, the donor **15** with bulky substituent group at C-3 might be not favourite for the acceptor erythronolide.

When the benzyl group was tried to modify the 6-OH group of compound **14** by using Ag_2O and BnBr, no product was obtained.[16] The Fmoc group of **14** was destroyed when NaH was used as the alkali (Scheme 3). The failure of glycosidation with **15** and modification of **14** forced us to revise our previous procedure.



Scheme 3. Reagents and conditions: a) NIS, AgOTf, CH_2Cl_2; b) Ag_2O or NaH, BnBr, DMF.

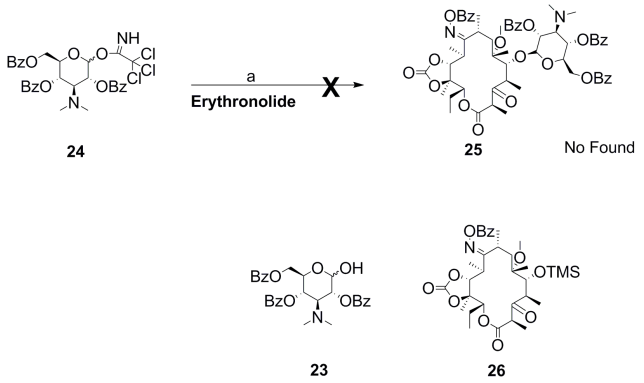
The synthetic route was adjusted as shown in Scheme **4**. Replacement the 3-NHFmoc group with 3-NMe_2 group of the donor was considered because of its relatively less steric hindrance. At the same time, trichloroacetimidate donor was also preferred because of its higher reactivity. Using this strategy, the target compound could be obtained directly after glycosylation. The synthetic route was adjusted from compound **10**, protection with BzCl formed compound **19** in a yield of 86%. Then, 6-OTBDPS group was selectively removed to form compound **20** which could be modified properly at 6-OH group. Benzoyl group was chosen as well and introduced with BzCl to obtain compound **21**. After that, hydrolysis of thioglycoside **21** with NBS formed compound **22** in acetone and H_2O in 85% yield.[17] The condition of Zn and acetic acid was adopted to reduce 3-N_3 group of compound **22** and methylation of 3-NH_2 with CH_3I was ongoing in a consecutive reaction in a yield of 49% for two steps.[18] The donor **24** was produced by the reaction of compound **23** with CCl_3CN and DBU in 91% yield.[19]



Scheme 4. Reagents and conditions: a) BzCl, pyridine, 86%; b) HCl, MeOH, 90%; c) BzCl, pyridine, 90%; d) NBS, acetone, H_2O, 85%; e) Zn, CH_3COOH, then, CH_3I, Na_2CO_3, DMF, two steps, 49%; f) CCl_3CN, DBU, CH_2Cl_2, 91%.

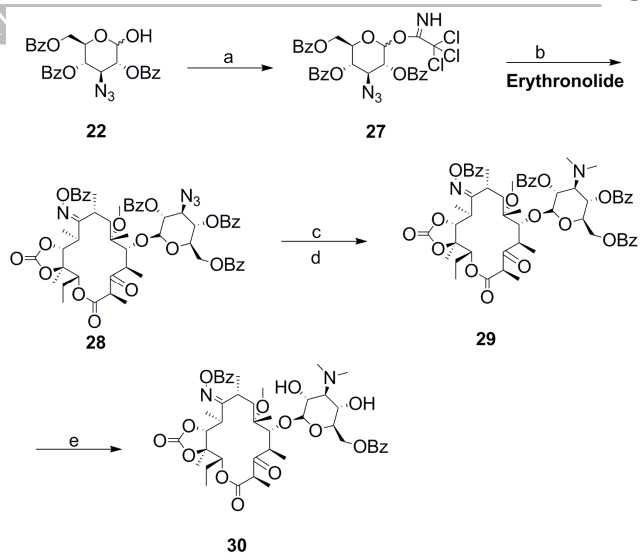
With the donor **24** obtained, glycosidation was tried again. TMSOTf was used as a promoter to couple the donor **24** with the acceptor erythronolide (Scheme 5). The molar ratio of TMSOTf

was 1.1 eq to the acceptor because of 3-NMe_2 group which acted as an acid-capturer.[4] It was also disappointed that the glycosidation was not successful. The donor **24** was much too unstable to form compound **23** in the presence of excess TMSOTf, while we reduced the molar ratio of TMSOTf to 0.1eq, no compound **25** was found. The main products were unreacted erythronolide and compound **23** when the reaction time extended to 24 hours. Compound **26** was also detected with HRMS $[M+H]^+$ 648.3150, $[M+Na]^+$ 670.2996. Considering the effect of the basicity of 3-NMe_2 group on the glycosidation, the ratio of TMSOTf was hard to control to balance the contradictory of reactivity and stability of the donor in the presence of 3-NMe_2 group.



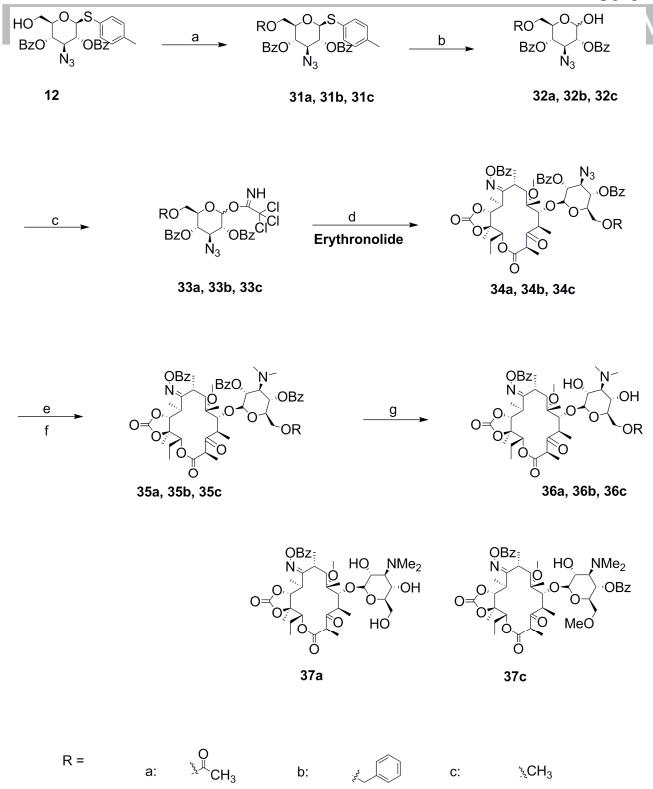
Scheme 5. Reagents and conditions: a) TMSOTf, CH_2Cl_2.

Aiming at avoiding the adverse influence of 3-NMe_2 group for glycosidation, 3-N_3 group was taken as the protective group which could be converted into 3-NMe_2 group by reduction and methlylation. The synthetic route was revised as followed (Scheme 6). Compound **22** was directly reacted with CCl_3CN and DBU to form donor **27** in 86% yield. Erythronolide was successfully glycosylated with donor **27** to afford the glycosylated product **28** in a yield of 31% using TMSOTf as a promoter, the structure was confirmed by ^{1}H NMR, ^{13}C NMR and HRMS spectra (H-1′ : 4.83 ppm, J = 7.6 Hz, β-configuration; C-1′ : 100.7 ppm; HRMS $[M+H]^+$ 1075.4110). Compound **29** was obtained with a consecutive reaction through reduction of 3′-N_3 group of compound **28** and followed by methylation of newly generated 3′-NH_2 group later in 50% yield for two steps, 3′-NMe_2 group was proved by the ^{1}HNMR signals (2.36 ppm, s, 6H). 2′- and 4′-OBz groups of compound **29** were removed in MeOH under reflux condition to obtain the target compound **30** in a yield of 70%, the ^{1}HNMR signals for H-2′ (5.30 ppm) and H-4′ (5.35 ppm) of compound **29** disappeared and shifted upfield, Which showed 2′-OBz group and 4′-OBz group were removed. This result was consistent with the work as Liang et al and Y, Xu et al reported, transesterification was easier to take place for 2′-OBz group and 4′-OBz group compared with 6′-OBz group and 9-N=OBz group. Up to now, with the adjustment of protective strategies and conditions of glycosidation, a new procedure was developed to obtain the target **30** designed via 18 steps in a total yield of 4%.



Scheme 6. Reagents and conditions: a) CCl_3CN, DBU, CH_2Cl_2 86%; b) TMSOTf, CH_2Cl_2, 31%; c) Lindlar catalyst, H_2, MeOH; d) CH_3I, Na_2CO_3, DMF, two steps yield 50%; e) MeOH, reflux, 70%.

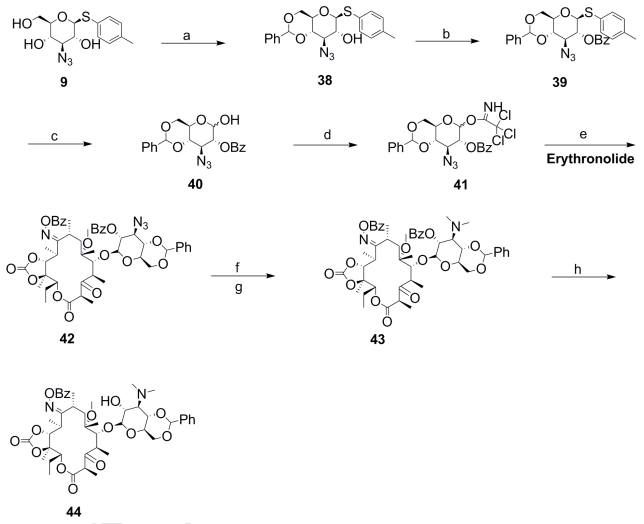
In order to estimate the practicability of the synthetic method aboved, different types of substituted groups for C-6′ were tried. Alkyl ester group (acetyl group) and ether group (benzyl group and methyl group) were explored to be introduced to C6′-modified ketolides which have never been reported before (Scheme 7). Acetyl group was introduced as a similar method for compound **21**, protection of compound **20** with Ac_2O in pyridine formed compound **31a** in a yield of 87%. Benzyl group was introduced with Ag_2O and BnBr from compound **20** in a yield of 73%.[16] Methyl group was introduced with Ag_2O and MeI as the method for compound **31b** in a yield of 70%. Then the donors **33a**, **33b** and **33c** were obtained as the method for donor **27** via two steps. Similarly, TMSOTf was used as a promoter to couple donor **33a, 33b** or **33c** with the acceptor erythronolide respectively to develop the compound **34a**, **34b** and **34c**, the yield was 58% for **34a**, 46% for **34b** and 68% for **34c**. The different yields of glycosidation showed that C6-alkly group modified donors **31a** and **31c** might be favored compared to the donors **27**, **31b** with aryl group modified at C-6 and donors **31b** and **31c** with electron-donating group at C-6 might also be beneficial compared to donors **27**, **31a** with electron-withdrawing groups. Compounds **35a**, **35b** and **35c** were formed via two steps through reduction of 3′-N_3 group and followed by methylation of newly generated 3′-NH_2 group later. Deprotection of 2′-OBz group and 4′-OBz group in MeOH at 70℃ produced the target compounds **36a**, **36b** and **36c**. Fortunately, 6′-deacetyl compound **37a** and **37c** were also separated. The structures of all compounds were confirmed by by ^{1}HNMR, ^{13}CNMR and HRMS spectra. Herein, ester groups (aryl group: benzoyl group and alkyl group: acetyl group) and ether groups (aryl group: benzyl group and alkyl group: methyl group) were successfully introduced to C-6’ ketolides with the procedure for compound **30**.



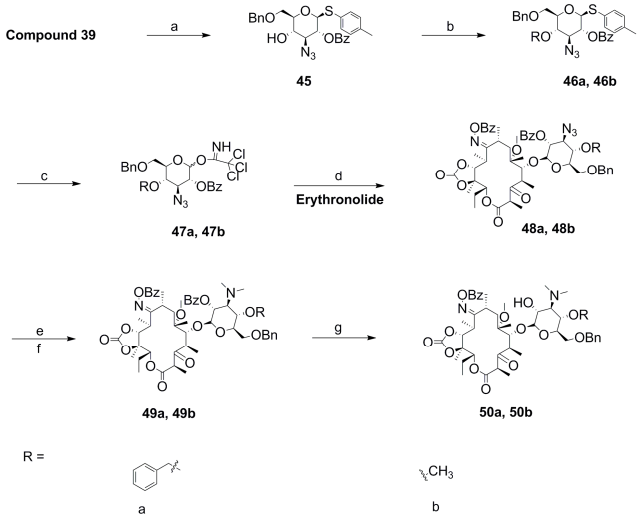
Scheme 7. Reagents and conditions: a) Ac_2O, Pyridine for 31a, 87%; Ag_2O, BnBr, DMF for 31b 73%; Ag_2O, MeI, DMF for 31c, 70%; b) NBS, acetone, H_2O; c) CCl_3CN, DBU, CH_2Cl_2 58% - 63% for two steps ; d) TMSOTf, CH_2Cl_2, 58% for 34a, 46% for 34b, 68% for 34c; e) Lindlar catalyst, H_2, MeOH; f) CH_3I, Na_2CO_3, DMF, two steps yield 70% for 35a, 50% for 35b, 71% for 35c; g) MeOH, reflux,44% for 36a, 62% for 36b, 35% for 36c, 40% for 37a, 40% for 37c.

C4′, C6′- benzal substituted ketolide was also synthesized here as a similar procedure (Scheme **8**). C4, C6- hydroxyl groups were protected by benzal group with 4-methylbenzenesulfonic acid and $PhCH(OMe)_2$ in a yield of 71%.[20] Then protection of 2-OH group with BzCl formed compound **39** in 71% yield. It was different that hydrolysis of thioglycoside **39** was proceeded under the condition of NIS/ CH_2Cl_2 / TFA / H_2O to produce compound **40** in a yield of 55%, while the condition of NBS / acetone / H_2O didn't work.[21,22] Compound **41** was obtained from compound **40** by the reaction with CCl_3CN and DBU in a yield of 96%. After that, according to the same procedure, the donor **41** was coupled with erythronolide in a yield of 60%. Then, 3′-N_3 group of compound **42** was converted to 3′-NMe_2 group in a consecutive reaction, the yield of two steps was 60%. C4′, C6′- benzal substituted ketolide **44** was obtained successfully from compound **43** in methanol under refluxing condition. C4′, C6′-dibenzyl substituted ketolide **50a** and C4′-methyl -C6′-benzyl substituted ketolide **50b** were also synthesized as a similar procedure (Scheme 9) here. Selective cleavage of the benzylidene group formed compound **45** in a yield of 56%.[23] The 4-OH group was modified with BnBr or MeI under the condition of NaH / DMF formed compound **46a**, **46b** respectively. The donors **47a** and **47b** were obtained via two steps same as the donor **41**. Similarly, the donors 47a, 47b were coupled with erythronolide respectively, the yield was 70% for **48a**, 62% for **48b**. Then, 3'-N_3 group was converted to 3′-NMe_2 group in a consecutive reaction, the yield of two steps was 70% for **49a**, 65% for **49b**.

Two novel ketolides **50a** and **50b** were obtained in methanol under refluxing condition in a yield of 55% and 69%. With this, Nine novel ketolides have been successfully synthesized which included several types of substituent groups at the C6′ of 5-*O*-desosamine mimetics. At the same time, the synthetic way was proved to have excellent practicability.



Scheme 8. Reagents and conditions: a) 4-methylbenzenesulfonic acid, $PhCH(OMe)_2$, DMF, 71%; b) BzCl, pyridine, 71%; c) NIS, CH_2Cl_2, H_2O, TFA, 55%; d) CCl_3CN, DBU, CH_2Cl_2, 96%; e) TMSOTf, CH_2Cl_2, 60%; f) Lindlar catalyst, H_2, MeOH; g) CH_3I, Na_2CO_3, DMF, two steps yield 60%; h) MeOH, reflux, 65%.



Scheme 9. Reagents and conditions: a) Et_3SiH, TFA, CH_2Cl_2, 56%; b) NaH, DMF, BnBr for 46a, 99%; MeI for 46b, 99%; c) NIS, CH_2Cl_2, H_2O, TFA, then CCl_3CN, DBU, CH_2Cl_2, two steps, 53% for 47a, 31% for 47b; e) TMSOTf, CH_2Cl_2, 70% for 48a, 62% for 48b; f) Lindlar catalyst, H_2, MeOH; g) CH_3I, Na_2CO_3, DMF, two steps yield 70% for 49a, 65% for 49b; h) MeOH, reflux, 55% for 50a, 69% for 50b.

3. Conclusion

In conclusion, an efficient procedure was developed by adjustment of protective strategies and glycosylation conditions. A series of novel ketolides were successfully synthesized which had different types of substituent groups at C-6′ of desosamine-mimetics. This work should offer us an opportunity to design more novel 5-*O*-(6′-modified)-desosamine-mimetics ketolides which could be contributed to a better understanding the SARs of desosamine

4. Experimental section

4.1. General

All solvents and reagents were obtained from commercial sources and used without further purification unless otherwise noted. All NMR spectra were recorded on Mercury-300, 400, 500 or 600 MHz spectrometers in $CDCl_3$ and CD_3OD. HRMS experiments were done with an Aglient 1100series LC/MSD TOF and MS with an Thermo-Finnigan LCQ Advantage. Analytical thin chromatography (TLC) was carried out on TLC plates silica gel HSGF254 percolated by Branch of Qingdao Haiyang Chemical Plant. Chromatography was performed with silica gel H (HG/T2354-92).

*4.2. Synthesis of 1,2: 5,6 -di-O-isopropylidene-α-D-allofuranose **3***

Compound **1** (13.0 g, 0.05 mol) in 80 mL CH_2Cl_2 was stirred at 0℃, Dess-Martin oxidant (35.0 g, 0.08 mol) was added in batches. After stirring for 2 hours at 0℃, the reaction solution was warmed up to room temperature and kept stirring for 20 hours. Then 80 mL saturated $NaHCO_3$ and 9.6 g $Na_2S_2O_3$ were added and stirred intensely. Organic phase was concentrated and dissolved in 100 mL ethanol. $NaBH_4$ (1.9 g, 0.05 mol) was dissolved in the mixture solution of ethanol / H_2O (20 mL / 20 mL) and dropped slowly to the reaction solution at 0℃. After that, kept stirring for 4 hours at room temperature, saturated NH_4Cl was added to quench the reaction and ethyl acetate was used to extracte. The organic phase was washed with brine, dried over anhydrous Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 5 : 1) to give compound **3** (10.4 g), the yield of two steps is 80%. ^{1}H NMR($CDCl_3$, 400 MHz): δ5.78 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 4.58 (dd, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 5.2 Hz, 1H, H-2), 4.29 (ddd, $J_{5,6a}$ = 4.8 Hz, $J_{5,6b}$ = 6.4 Hz, $J_{5,4}$ = 6.4 Hz, 1H, H-5), 3.97-4.08 (m, 3H, H-3, H-4, H-6a), 3.80 (dd, $J_{6b,5}$ = 4.5 Hz, $J_{6b,6a}$ = 8.4 Hz, 1H, H-6b), 2.58 (br, 1H, 3-OH), 1.55, 1.44, 1.36, 1.34 (4 × s, 4 × 3H,). ^{13}C NMR($CDCl_3$, 100MHz): δ 112.7, 109.7, 103.8, 79.6, 78.8, 75.5, 72.4, 65.7, 26.5, 26.4, 26.2, 25.2. ESI-MS: calcd for $C_{12}H_{20}NaO_6$ $[M+Na]^+$ 283.1260, found: 283.1169

*4.3. Synthesis of 1,2: 5,6-di-O-isopropylidene-3-O-triflyl-α-D-allofuranose **4***

A solution of compound **3** (20.0 g, 0.08 mol) in 24 mL pyridine under argon was cooled to 0℃. Tf_2O (20.3 mL, 0.12 mol) was added in. After stirring 3.5 hours at room temperature, the reaction mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : CH_2Cl_2 = 1 : 1) to give compound **4** (28.6g) with a yield of 95%. ^{1}H NMR($CDCl_3$, 300 MHz): δ5.83 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 4.90 (dd, $J_{3,4}$ = 6.3 Hz, $J_{3,2}$ = 5.7 Hz, 1H, H-3), 4.76 (dd, $J_{2,3}$ = 4.8 Hz, $J_{2,1}$ = 4.2 Hz, 1H, H-2), 4.08-4.20 (m, 3H, H-6b, H-4, H-6a), 3.90 (dd, $J_{5,6a}$ = 4.5 Hz, $J_{5,6b}$ = 8.7 Hz, 1H, H-5), 1.58, 1.44, 1.38, 1.34 (4 × s, 4 × 3H). ^{13}C NMR($CDCl_3$, 75MHz): δ118.6,114.4, 110.3, 104.1, 82.3, 77.8, 77.7, 75.2, 66.3, 26.8, 26.5, 26.2, 24.8. ESI-MS: calcd for $C_{13}H_{20}F_3O_8S$ $[M+H]^+$ 393.0753, found: 393.0807.

*4.4. Synthesis of 1,2: 5,6-di-O-isopropylidene-3-azido-3-deoxy-α-D-allofuranose **5***

NaN_3 (3.3 g, 0.05 mol) was added to a solution of compound **4** in 24.0 mL DMF. After stirring for 6 hours at 50℃, the reaction solution was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 12 : 1) to give compound **5** (12.6 g, 99%). ^{1}H NMR($CDCl_3$, 400 MHz): δ5.85 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 4.61 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-2), 4.24 (m, 1H), 4.08-4.16 (m, 3H), 4.00 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{5,6b}$ = 8.8 Hz, 1H, H-5), 1.51, 1.43, 1.37, 1.32 (4 × s, 4 × 3H). ^{13}C NMR($CDCl_3$, 100MHz): δ112.2, 109.5, 110.3, 105.0, 80.4, 72.9, 67.6, 66.2, 26.8, 26.5, 26.3, 25.1. ESI-MS: calcd for $C_{12}H_{20}N_3O_5$ $[M+H]^+$ 286.1325, found: 286.1380.

*4.5. Synthesis of 1,2,4,6-tetra-O-acetyl-3-azido-3-deoxy-α,β-D-glucopyranose **7***

Compound **5** (3.1 g, 0.01 mol) was dissolved in a mixture solution of 20 mL TFA and 3 mL H_2O. After stirring for 2 hours at room temperature, the reaction solution was concentrated and dissolved with 60 mL pyridine. Added Ac_2O (49.7 g, 0.49 mol) and kept stirring for 20 hours. The reaction solution was concentrated and diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 5 : 1) to give compound **7** (9.4 g, 80%, α / β = 1 : 0.4). ^{1}H NMR($CDCl_3$, 300 MHz, α / β = 1 : 0.4): δ6.29 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1$_\alpha$), 5.67 (d, $J_{1,2}$ = 8.5 Hz, 0.4H, H-1$_\beta$), 4.98-5.05 (m, 1.8H), 4.95 (dd, J_1 = 3.6 Hz, $J_{2,1}$ = 10.8 Hz, 1H), 4.18-4.26 (m, 1.4H), 4.02-4.12 (m, 2.4H), 3.96 (t, J = 10.5Hz, 1H), 3.75-3.80 (m, 0.4H), 3.68 (t, J = 10.5 Hz, 0.4H), 2.18, 2.13 (2× s, 2 × 3H), 2.12, 2.11, 2.10 (3 × s, 3 × 3H), 2.08 (s, 7.17H). ESI-MS: calcd for $C_{14}H_{24}N_4O_{10}$ 391.1121, found: 391.1478 [M + NH_4^+].

*4.6. Synthesis of p-methylphenyl-2,4,6-tri-O-acetyl-3-azido-3-deoxy-1-thio-β-D-glucopyranoside **8***

4-Methylthiophenol (1.3 g, 1.00 mmol) was added to a solution of compound **7** (3.5 g, 9.30 mmol) dissolved in 10 mL anhydrous CH_2Cl_2. Then 3.5 mL $BF_3{\cdot}Et_2O$ was dropped slowly. After stirring for 12 hours at 40℃, the reaction solution was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 7 : 1) to give compound **8** (3.6 g, β, 87%). ^{1}H NMR($CDCl_3$, 400 MHz): δ7.39 (d, J = 8.0Hz, 2H), 7.12 (d, J = 8.0Hz, 2H), 4.91 (t, J = 10.0 Hz, 1H, H-2), 4.87 (t, J = 10.0 Hz, 1H, H-4), 4.59 (d, J = 9.6 Hz, 1H, H-1), 4.16-4.17 (m, 2H, H-6b, H-6a), 3.62-3.76 (m, 2H, H-5, H-3), 2.29 (s, 3H), 2.18, 2.11, 2.08 (3× s, 3× 3H). ^{13}C NMR($CDCl_3$, 100 MHz): δ170.8, 169.4, 169.3, 139.0, 133.8, 129.9, 128.1,86.6, 76.6, 70.2, 68.5, 66.0, 62.4, 21.4, 21.1, 21.0, 20.9. ESI-MS: calcd for $C_{19}H_{28}N_4O_8S$ 455.1257, found: 455.1568 [M + NH_4^+].

*4.7. Synthesis of p-methylphenyl-3-azido-3-deoxy-1-thio-β-D-mannopyranoside **9***

Compound **8** (1.8 g, 4.11 mmol) was dissolved in 20 mL methanol and added MeONa (0.2 g, 4.00 mmol) under argon. After stirring for 4 hours at room temperature, the reaction solution was neutralized with AMBERLYST(R) 15 and filtered. The concentrate was purified by column chromatography (MeOH : CH_2Cl_2 = 60 : 1) to give compound **9** (1.2 g, 95%). ^{1}H

NMR(CD_3OD, 400 MHz): δ7.44 (d, *J* = 8.0Hz, 2H), 7.10 (d, *J* = 8.0Hz, 2H), 4.53 (d, *J* = 9.6 Hz, 1H, H-1), 3.84 (dd, $J_{6a, 6b}$ = 12.0 Hz, $J_{6a, 5}$ = 2.0 Hz, 1H, H-6a), 3.65 (dd, $J_{6a, 6b}$ = 12.0 Hz, $J_{6b, 5}$ = 5.2 Hz, 1H, H-6b), 3.32 (m, 2H, H-2, H-5), 3.25 (t, *J* = 9.6Hz, 1H, H-4), 3.17 (t, *J* = 9.6Hz, 1H, H-3), 2.30 (s, 3H). ^{13}C NMR(CD_3OD, 100 MHz): δ137.8, 132.5, 129.6, 129.4,88.7, 81.2, 71.8, 71.5, 68.8, 61.4, 19.9. ESI-MS: calcd for $C_{13}H_{17}N_3NaO_4S$ $[M+Na]^+$ 334.0940, found: 344.0799.

4.8. Synthesis of p-methylphenyl-3-azido-3-deoxy-6-O-tertbutyl-diphenylsilyl-1-thio-β-D-glucopyranoside ***10***

Compound **9** (2.8 g, 9.11 mmol) was dissolved in 10 mL pyridine. TBDPSCl (2.9 g, 10.60 mmol) and DMAP (300.0 mg) were added. After stirring for 5 hours at room temperature, the reaction solution was concentrated and diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 5 : 1) to give compound **10** (4.6 g, 92%). ^{1}H NMR($CDCl_3$, 400 MHz): δ 7.69-7.72 (m, 4H), 7.40-7.49 (m, 8H), 7.09 (d, *J* = 8.0Hz, 2H), 4.45 (d, *J* = 9.6 Hz, 1H, H-1), 3.94 (m, 2H, H-6a, H-6b), 3.58 (dd, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 1H, H-2), 3.50 (m, 2H, H-3, H-5), 3.31 (dd, J_1 = 2.4 Hz, J_2 = 9.6 Hz, 1H, H-4), 2.91, 2.55 (2 × OH, d, J = 2.4 Hz), 2.33 (s, 3H), 1.07(s, 9H, $(CH_3)_3C$). ^{13}C NMR($CDCl_3$, 100 MHz): δ 138.8, 135.6, 135.5, 133.7, 132.6, 132.5, 130.0, 129.9, 129.8, 127.9, 127.8, 126.7, 88.3, 79.0, 70.8, 70.6, 69.5, 64.3, 26.6, 21.1, 19.1. ESI-MS: calcd for $C_{29}H_{35}N_3NaO_4SSi$ $[M+Na]^+$ 572.2118, found: 572.2008.

4.9. Synthesis of p-methylphenyl-3-amino-3-deoxy-6-O-tertbutyl-diphenylsilyl-1-thio-β-D-glucopyranoside ***11***

PPh_3 (665.0 mg, 2.50 mmol) and H_2O (220.0 mg, 12.20 mmol) were added to a solution of compound **10** dissolved in 5 mL THF under argon. After stirring for 24 hours under refluxing condition. The reaction solution was concentrated and purified by column chromatography (PE : EtOAc = 3 : 1) to give compound **11** (417.0 mg, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (m, 4H), 7.40(m, 8H), 7.00 (d, *J* = 7.6 Hz, 2H), 4.45 (d, *J* = 9.6 Hz,1H, H-1) , 4.10 (dd, J_1 = 12.0 Hz, J_2 = 7.6 Hz, 1H, H-6), 3.93 (m, 2H), 3.42 (m, 2H), 3.12 (dd, J_1 = 9.6 Hz, J_2 = 9.2 Hz, 1H), 2.66 (br, 2H), 2.31 (s, 3H), 1.07 (s, 9H). ESI-MS: calcd for $C_{29}H_{38}NO_4SSi$ $[M+H]^+$ 524.2213, found: 524.2445.

4.10. Synthesis of p-methylphenyl-6-O-tertbutyldiphenylsilyl-3-fluorenylmethoxy-carbony-amino-3-deoxy-1-thio-β-D-glucopyranoside ***12***

Compound **11** (102.0 mg, 0.20 mmol) was dissolved in 3 mL CH_2Cl_2 with 0.6 mL saturated $NaHCO_3$ solution. Then FmocCl (76.0 mg. 0.30 mmol) was added. After stirring for 3 hours at room temperature, the reaction solution was washed with brine, concentrated and purified by column chromatography (PE : EtOAc = 5 : 1) to give compound **12** (112.0 mg, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (m, 6H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.41 (m,10H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 7.2 Hz, 2H), 4.49 (d, *J* = 9.4 Hz, 1H) , 4.43 (d, *J* = 6.8 Hz, 2H), 4.21 (m, 1H), 3.95 (m, 2H), 2.35 (s, 3H), 1.07 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 141.5, 138.5, 135.8, 135.8, 133.6, 133.2, 130.0, 129.9, 128.0, 127.9, 127.3, 125.2, 120.2, 88.9, 80.7, 70.5, 67.5, 64.4, 61.4, 47.3, 27.0, 21.3, 19.4. ESI-MS: calcd for $C_{44}H_{48}NO_6SSi$ $[M+H]^+$ 746.2893, found: 746.3051.

4.11. Synthesis of p-methylphenyl-2,4-di-O-benzoyl-6-O-tertbutyl-diphenylsilyl-3-fluorenylmethoxycarbonyamino-3-deoxy-1-thio-β-D-glucopyranoside ***13***

BzCl (139.0 mg, 0.66 mmol) was added to a solution of compound **12** (246.0 mg, 0.30 mmol) in 5 mL pyridine under argon condition. After stirring for 5 hours at room temperature, the reaction solution was concentrated and diluted with CH_2Cl_2, the diluent was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 10 : 1) to give compound **13** (254.0 mg, 81%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07 (d, *J* = 7.6 Hz, 2H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.51 (d, *J* = 7.2 Hz 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.38 (m, 7H), 7.30 (m, 5H), 7.14 (m, 4H), 7.07 (d, *J* = 7.2 Hz, 2H), 5.45 (t, *J* = 9.6 Hz, 1H), 5.21 (d, *J* =10.0 Hz, 1H), 5.15 (t, *J* =10.0 Hz, 1H), 4.95 (d, *J* = 9.6 Hz, 1H), 4.50 (t, *J* = 10.0 Hz, 1H), 3.87-3.94 (m, 5H), 3.72 (t, *J* = 9.6 Hz, 1H), 2.35 (s, 3H), 1.06 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) 166.0, 166.0, 156.4, 143.9, 143.9, 141.2, 138.8, 135.9, 135.7, 134.4, 133.6, 133.5, 133.0, 131.1, 130.3, 130.2, 129.9, 129.8, 129.6, 129.4, 129.1, 128.6, 128.6, 127.9, 127.8, 127.6, 127.1, 125.3, 119.9, 86.6, 80.2, 71.3, 68.9, 67.4, 62.7, 58.1, 47.0, 26.8, 21.4, 19.4. ESI-MS: calcd for $C_{58}H_{56}NO_8SSi[M+H]^+$ 954.3418, found: 954.3406.

4.12. Synthesis of p-methylphenyl-2,4-di-O-benzoyl-3-fluorenyl methoxycarbonyamino-3-deoxy-1-thio-β-D-glucopyranoside ***14***

Compound **13** (32.0 mg, 0.03 mmol) dissolving in 1 mL MeOH was added 0.1 mL concentrated hydrochloric acid. After stirring for 12 hours at room temperature. The reaction solution was washed with $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 20 : 1) to give compound **14** (19.0 mg, 79%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.45 (m, 3H), 7.34 (m, 7H), 7.13 (m, 2H), 7.12 (d, *J* = 7.2 Hz, 2H), 7.08 (d, *J* = 7.6 Hz, 2H), 5.24 (t, *J* = 9.6 Hz, 1H), 5.10 (t, *J* = 10.0 Hz, 1H), 4.96 (d, *J* = 9.6 Hz, 1H), 4.50 (q, *J* = 10.4 Hz, 1H), 4.30 (t, *J* = 6.8 Hz, 1H), 3.94 (m, 1H), 3.83 (m, 2H), 3.72 (m, 2H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.6, 166.1, 156.4, 143.8, 141.6, 139.1, 134.2, 133.9, 133.7, 131.1, 130.3, 130.0, 129.4, 129.1, 128.9, 128.7, 128.6, 127.7, 127.1, 125.2, 119.9, 86.7, 79.7, 71.1, 69.6, 67.5, 61.9, 57.5, 46.9, 21.4, 19.4. ESI-MS: calcd for $C_{42}H_{38}NO_8S$ $[M+H]^+$ 716.2240, found: 716.2401.

4.13. Synthesis of p-methylphenyl-2,4,6-tri--O-benzoyl-3-fluorenylmethoxycarbony amino-3-deoxy- 1-thio-β-D-glucopyranoside ***15***

BzCl (40 mg, 0.30mol) was added to a solution of compound **14** dissolved in 2 mL pyridine under argon condition. After stirring for 5 hours , the reaction solution was concentrated and diluted with CH_2Cl_2. The diluent was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 12: 1) to give compound **15** (116.0 mg, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (m, 4H), 7.98 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 3H), 7.26-7.41 (m, 10H), 7.11 (m, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 5.34 (dd, J_1, J_2 = 10.0 Hz , 1H, H-2), 5.14 (dd, J_1, J_2 = 9.6 Hz, 1H, H-4), 5.09 (m, 1H, H-5), 4.98 (d, *J* = 9.6 Hz, 1H, H-1), 4.70 (d, *J* = 11.6 Hz, 1H, H-6a), 4.51 (dd, J_1, J_2 = 10.0 Hz , 1H, H-3), 4.44 (m, 1H, H-6b), 4.17 (br, 1H), 3.93 (d, *J* = 7.6 Hz, 2H), 3.68 (t, *J* = 7.2 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 166.1, 156.4, 134.6, 133.4, 130.3, 130.2, 130.1, 129.8, 128.6, 127.7, 127.1, 125.2, 119.9, 110.0, 86.5, 77.2, 70.8,

69.6, 67.5, 63.2, 57.8, 46.9, 21.4. ESI-MS: calcd for $C_{49}H_{42}NO_9S$ [M+H]$^+$ 820.2502, found: 820.2541.

*4.14. Synthesis of p-methylphenyl-3-azido-3-deoxy-2,4-di-O-benzoyl-6-O-tert-butyldiphenylsilyl-1-thio-β-D-gluco-pyranoside **19***

To a solution of compound **10** (206.0 mg, 0.40 mmol) in 3 mL pyridine under argon was added BzCl (160.0 mg, 1.10 mmol). After stirring for 6 hours. The solution was concentrated and diluted with CH_2Cl_2. The diluent was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 10 : 1) to give compound **19** (244.2 mg, 86%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, *J* = 8.0Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.61 (m, 4H), 7.48 (m, 6H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 3H), 7.19 (t, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 5.37(dd, J_1, J_2 = 10.0 Hz, 9.6 Hz, 1H, H-2), 5.22 (dd, J_1, J_2 = 10.0 Hz, 9.6 Hz , 1H, H-4), 4.89 (d, *J* = 9.6 Hz, 1H, H-1), 3.98 (dd, J_1, J_2 = 10.0 Hz, 9.6 Hz, 1H, H-5), 3.80 (m, 3H, H-6a, H-6b, H-3), 2.32 (s, 3H), 1.04 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.1, 164.9, 138.7, 133.8, 133.7, 133.1, 133.1, 130.2, 130.1, 129.9, 129.8, 129.6, 129.3, 128.7, 128.5, 127.9, 127.8, 127.8, 86.9, 80.0, 71.1, 69.1, 66.7, 63.0, 26.9, 21.4, 19.4. ESI-MS: calcd for $C_{43}H_{44}N_3O_6SSi$ [M+H]$^+$ 758.2642, found:758.2619.

*4.15. Synthesis of p-methylphenyl-3-azido-3-deoxy-2,4-di-O-benzoyl-1-thio-β-D-glucopyranoside **20***

0.2 mL concentrated hydrochloric acid was added to a solution of compound **19** (120.0 mg, 0.16 mmol) in 1 mL MeOH. After stirring for 10 hours, the solution was washe with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 10 : 1) to give compound **20** (74.0 mg, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.2 Hz, 2H), 8.03 (d, *J* = 7.8 Hz, 2H), 7.62 (m, 2H), 7.49 (m, 4H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 5.19 (d, J_1 = 9.1 Hz, J_2 = 8.7 Hz, 1H), 5.17 (d, J_1 = 9.1 Hz, J_2 = 8.7 Hz, 1H), 4.86 (d, *J* = 9.9 Hz, 1H, H-1), 4.05 (dd, J_1, J_2 = 9.9 Hz, 9.8 Hz, 1H), 3.79 (dd, J_1, J_2 = 9.9 Hz, 9.4 Hz, 1H), 3.70 (m, 2H), 2.34 (s, 3H). ESI-MS: calcd for $C_{27}H_{26}N_3O_6S$ [M+H]$^+$ 520.1464, found: 520.1478.

*4.16. Synthesis of p-methylphenyl-3-azido-3-deoxy-2,4,6-tri-O-benzoyl-1-thio-β-D-glucopyranoside **21***

Compound **20** (49.0 mg, 0.10 mmol) was dissolved in 1 mL pyridine, then BzCl (20.0 mg, 0.14 mmol) was added. After stirring for 1 hour, the solution was concentrated and diluted with CH_2Cl_2. The diluent was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 20 : 1) to give compound **21**(53.0 mg, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, *J* = 8.0 Hz, 2H), 8.02 (t, *J* = 7.2 Hz, 4H), 7.62 (t, *J* = 7.2 Hz, 1H),7.56 (t, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.43 (m, 4H), 7.36 (t, *J* = 8.0 Hz, 2H), 6.91 (t, *J* = 8.0 Hz, 2H), 5.34 (dd, J_1, J_2 = 10.0 Hz, 1H, H-2), 5.20 (dd, J_1, J_2 = 10.0 Hz, 9.6 Hz, 1H, H-4), 4.88 (d, J_1 = 10.0 Hz, 1H, H-1), 4.63 (m, 1H, H-6a), 4.34 (dd, J_1, J_2 = 12.0 Hz, 6.0 Hz,1H, H-6b), 4.05 (m, 2H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 165.1, 165.1, 138.9, 134.0, 133.8, 133.4, 130.2, 130.2, 130.1, 129.8, 129.4, 128.9, 128.8, 128.8, 128.6, 127.8, 86.7, 76.8, 70.9, 69.7, 66.5, 63.3, 21.4. ESI-MS: calcd for $C_{34}H_{30}N_3O_7S$ [M+H]$^+$ 624.1726, found: 624.1780.

*4.17. Synthesis of 3-azido-3-deoxy-2,4,6-tri-O-benzoyl-D-gluco-pyranoside **22***

Compound **21** (89.0 mg, 0.14 mmol) was dissolved in a mixture solution of 5 mL acetone and 0.5 mL H_2O. Then NBS (76.0 mg, 0.43 mmol) was added. After stirring overnight, the solution was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 10: 1) to give compound **22** (64.0 mg, 85%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.09 (t, *J* = 7.6 Hz, 4H), 8.01 (t, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 4H), 7.38 (t, *J* = 7.6 Hz, 2H), 5.68 (1H, dd, J_1 = 4.0 Hz, J_2 = 3.6 Hz ,H-1), 5.40 (t, *J* = 10.0 Hz, 1H, H-4), 5.05 (dd, J_1 = 10.4 Hz, J_2 = 4.0 Hz, 1H, H-2), 4.53-4.62 (m, 2H, H-6a, H-5), 4.44 (t, *J* = 10.4 Hz, H-3), 4.36 (dd, J_1 = 4.0 Hz, J_2 = 12.4, H-6b), 3.43 (d, *J* = 3.6, 1H, 1-OH). ^{13}C NMR($CDCl_3$, 100MHz) δ 166.5, 165.8, 165.2, 133.9, 133.4, 130.2, 130.0, 129.7, 129.1, 129.1, 128.8, 128.6, 90.0, 72.9, 69.65, 67.9, 63.0, 61.5. ESI-MS: calcd for $C_{27}H_{23}N_3NaO_8$[M + Na]$^+$ 540.1485. found: 540.1377.

*4.18. Synthesis of 2,4,6-tri-O-benzoyl- 3-dimethylamino-3-deoxy-D-glucopyranoside **23***

Compound **22** (200.0 mg, 0.40 mmol) was dissolved in 10 mL acetic acid. Excessive Zn powder was added in batches. After stirring for 2 hours, the reaction solution was filtered and the filtrate was diluted with CH_2Cl_2 , washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4. The concentrate was dissolved in 2 mL DMF with anhydrous sodium carbonate (43.0 mg, 0.40 mmol). Then, 0.5 mL CH_3I was added. After stirring overnight, the solution was washed with H_2O and extracted with CH_2Cl_2, organic layer was dried over Na_2SO_4. The concentrate was purified by column chromatography (PE : EtOAc = 6 : 1) to give compound **23** (97 mg, 49%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.09 (t, *J* = 7.2 Hz, 2H), 8.03 (t, *J* = 7.2 Hz, 4H), 7.51-7.60 (m, 3H), 7.37-7.47 (m, 6H), 5.57 (1H, H-1), 5.42 (t, *J* = 9.6 Hz, 1H, H-4), 5.28 (1H, H-2), 4.53-4.62 (m, 2H, H-6a, H-5), 4.38 (dd, J_1 = 4.0 Hz, J_2 = 11.6, H-6b), 3.59 (t, *J* = 10.4 Hz, H-3), 3.35(1H, 1-OH), 2.40 (s, 6H, NMe_2). ^{13}C NMR($CDCl_3$, 100MHz) δ 166.6, 165.8, 165.6, 133.6, 133.3, 133.2, 130.2, 130.1, 130.1, 123.0, 129.9, 128.7, 128.6, 128.5, 90.7, 70.4, 68.6, 67.8, 63.8, 62.5, 41.5. ESI-MS: calcd for $C_{29}H_{30}NO_8$ [M + H]$^+$ 520.1893, found: 520.1962.

*4.19. Synthesis of 2,4,6-tri-O-benzoyl- 3-dimethylamino-3-deoxy-D-glucopyranoside trichloroacetimidate **24***

Compound **23** (98.0 mg, 0.19 mmol) was dissolved in 2 mL anhydrous CH_2Cl_2 under argon at -10℃. Then CCl_3CN (274.3 mg, 1.90 mmol) was injected in. After stirring for 20 minutes, DBU (3.0 mg, 0.02 mmol) was injected in. Then reaction solution was warmed to room temperature and stirred for 5 hours. The reaction mixture was purified by column chromatography on silica gel (deactivated by 15% Et_3N/ PE) (PE : EtOAc = 20 : 1) to give compound **24** (114.0 mg. 91%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.55 (s,1H,C=NH),8.05 (t, *J* = 7.6 Hz, 4H), 8.00 (t, *J* = 8.4 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.44 (m, 6H), 6.67 (d, *J* = 3.6 Hz, 1H, H-1), 5.56 (dd, J_1 = 3.6 Hz, J_2 = 10.4, H-2), 5.51 (t, *J* = 10.4 Hz, 1H, H-4), 4.57 (1H, H-6a), 4.51 (m, 1H, H-5), 4.40 (dd, J_1 = 5.6 Hz, J_2 = 12.0, H-6b), 3.62 (t, *J* = 10.4 Hz, H-3), 2.42 (s, 6H, NMe_2).

*4.20. Synthesis of 3-azido-3-deoxy-2,4,6-tri-O-benzoyl-D-gluco-pyranoside trichloroacetimidate **27***

Compound **22** (1.7 g, 3.40 mmol) was dissolved in 20 mL anhydrous CH_2Cl_2 under argon at 0℃, CCl_3CN (4.9 g, 0.03 mol) was injected in. After stirring for 10 minuts, DBU (0.1 g, 0.7 mmol) was injected in. After stirring for 5 hours, the reaction

solution was purified by column chromatography on silica gel (deactivated by 15% Et_3N/ PE) (PE : EtOAc = 40 :1) to give compound **27** (1.9 g, 86%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.65 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.38-7.61 (m, 9H), 6.73 (d, *J* = 3.6 Hz, 1H, H-1), 5.50 (dd, J_1 = 10.4 Hz, J_2 = 10.0 Hz, H-4), 5.37 (dd, J_1 = 10.4 Hz, J_2 = 3.6 Hz, H-2), 4.58 (dd, J_1 = 12.4 Hz, J_2 = 2.4 Hz, H-6b), 4.51 (m, 1H, H-5), 4.44 (dd, J_1 = 10.4 Hz, J_2 = 10.0 Hz, H-3), 4.39 (dd, J_1 = 10.4 Hz, J_2 = 4.8 Hz, H-6a),

4.21. (E)-5-(3-azido-3-deoxy-2,4,6-tri-O-benzoyl-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***28***

Compound **27** (515.0 mg, 0.78 mmol) and compound erythronolide (193.0 mg, 0.34 mmol) were dissolved in 5 mL anhydrous CH_2Cl_2 under argon at -20℃， TMSOTf (15.0 mg, 0.07 mmol) was injected in. Then the reaction solution was warmed to room temperature and kept stirring for 12 hours. Trimethylamine (6.8 mg, 0.07 mmol) was added in and stirred for 20 minutes. Followed by filtration and purification by column chromatography (PE : EtOAc = 5 : 1) to give compound **28** (110.0 mg, 31%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 8.0 Hz, 2H), 8.05 (m, 5H), 7.60 (m, 3H), 7.46 (m, 10H), 5.37 (dd, J_1 = 10.0 Hz, J_2 = 9.6 Hz, 1H, H-4′), 5.30 (dd, J_1 = 10.0 Hz, J_2 = 8.0 Hz, 1H, H-2′), 5.02 (d, *J* = 9.6 Hz, 1H, H-13), 4.83 (d, *J* = 7.6 Hz, 1H, H-1′), 4.79 (s, 1H, H-11), 4.65 (d, *J* = 7.6 Hz, 1H, H-5), 4.40 (dd, J_1 = 12.0 Hz, J_2 = 6.8 Hz, H-6b), 4.20 (d, *J* = 7.6 Hz, 1H, H-2), 4.09 (m, 1H), 3.97 (dd, J_1 = 10.0 Hz, J_2 = 10.0 Hz, H-3′), 3.69 (m, 1H), 2.51 (s, 3H, 6-OMe), 1.43(s, 3H), 1.38 (d, *J* = 6.8 Hz, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 7.6 Hz, 3H), 0.84 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR($CDCl_3$, 100MHz) δ 203.6, 168.9, 166.1, 165.1, 164.6, 164.6, 153.8, 134.0, 133.8, 133.4, 133.4, 130.5, 130.1, 130.0, 129.9, 129.5, 129.2, 128.8, 128.7, 128.7, 128.6, 100.7, 85.4, 81.2, 79.6, 78.4, 77.4, 76.7, 73.1, 72.2, 69.8, 65.2, 62.9, 51.4, 49.2, 46.9, 38.0, 35.7, 33.8, 22.8, 19.5, 19.1, 15.5, 14.2, 13.9, 11.6, 10.5. HRMS (ESI) $[M+H]^+$ 1075.4188, calcd for $C_{57}H_{63}N_4O_{17}$, 1075.4110.

4.22. (E)-5-(2,4,6-tri-O-benzoyl- 3-dimethylamino-3-deoxy mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***29***

Compound **28** (60.0 mg, 0.06 mmol) was dissolved in 2 mL methanol, Lindlar catalyst (100 mg) was added in for hydrogenation under atmospheric pressure. After compound 28 was reacted completely, the catalyst was filtered and the filtrate was concentrated. Then concentrate was dissolved in 2 mL DMF with Na_2CO_3 (10.0 mg, 0.09 mmol). After stirring for 10 minutes, 0.5 mL CH_3I was added in and kept stirring for 10 hours. The reaction solution was diluted with CH_2Cl_2 and washed with H_2O, the organic phase was concentrated and purified by column chromatography on silica gel($CHCl_3$: PE : MeOH = 500 : 500 : 1) to give the compound **29** (32.0 mg, 50%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 7.95-8.04 (m, 8H), 7.60 (m, 3H), 7.46 (m, 7H), 7.32 (t, *J* = 7.6 Hz, 2H), 5.35 (dd, J_1 = 9.6 Hz, J_2 = 9.6 Hz, 1H, H-4′), 5.30 (dd, J_1 = 9.6 Hz, J_2 = 8.0 Hz, 1H, H-2′), 5.06 (dd, *J* = 10.0 Hz, 2.4 Hz, 1H, H-13), 4.84 (s, 1H, H-11), 4.80 (d, *J* = 8.0 Hz, 1H, H-1′), 4.49 (m, 2H), 4.24 (d, *J* = 7.6 Hz, 1H, H-2), 4.08 (m, 1H), 3.72 (m, 1H), 3.22 (dd, J_1 = 10.0 Hz, J_2 = 10.0 Hz, H-3′), 2.44 (s, 3H, 6-OMe), 2.36 (s, 6H, 3′-NMe_2), 1.39 (d, *J* = 6.8 Hz, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.30 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.8 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 175.2, 169.2, 166.2, 165.4, 164.8, 163.7, 153.8, 133.6, 133.4, 133.5, 130.2, 130.0, 129.9, 129.8, 129.6, 128.9, 128.8, 128.7, 128.6, 101.3, 77.1, 73.6, 70.7, 68.1, 76.9, 63.7, 51.3, 49.7, 41.5, 38.2, 29.9, 28.6, 22.8, 20.1, 14.4, 13.6, 10.5. HRMS (ESI) $[M+H]^+$ 1077.4586, calcd for $C_{59}H_{69}N_2O_{17}$, 1077.4518

4.23. (E)-5-(6-O- benzoyl- 3-dimethylamino-3-deoxy mycaminosy)

-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O(benzoyl) oxime 11,12-cyclic carbonate ***30***

Compound **29** (20.0 mg, 0.02 mmol) was dissolved in 2 mL methanol under refluxing condition for two days. The reaction solution was concentrated and purified by column chromatography on silica gel ($CHCl_3$: MeOH = 200 : 1) to give the compound **30** (10.7 mg, 70%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.97(d, *J* = 8.0 Hz, 2H), 7.59(t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 5.06 (d, *J* = 8.4 Hz, 1H, H-13), 4.83 (s, 1H, H-11), 4.66 (dd, J_1 = 12.0 Hz, J_2 = 6.4 Hz, H-6a′), 4.57 (d, *J* = 11.6 Hz, H-6b′), 4.46 (d, *J* = 7.2 Hz, 1H, H-1′), 4.23(m, 1H),3.84 (m, 1H), 3.69 (m, 1H), 2.63 (s, 6H, 3′-NMe_2), 2.51 (s, 3H, 6-OMe), 1.40 (t, *J* = 6.4 Hz, 6H), 1.35 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.0, 175.5, 165.9, 165.0, 163.5, 153.6, 133.5, 130.0, 129.8, 129.7, 128.8, 128.7, 128.7, 103.3, 84.8, 77.4, 76.6, 75.0, 70.7, 66.9, 64.3, 51.3, 49.9, 47.2, 41.9, 38.4, 29.9, 22.6, 20.0, 18.9, 15.6, 14.6, 13.6, 10.6, 10.5. HRMS (ESI) $[M+H]^+$ m/z 869.3999, calcd for $C_{45}H_{60}N_2O_{15}$, 869.3994.

4.24. Synthesis of p-methylphenyl-6-O-acetyl-3-azido-3-deoxy-2,4-di-O-benzoyl-1-thio-β-D-glucopyranoside ***31a***

Compound **31a** (912.9mg, 87%) was obtained from compound **20** (971.0 mg, 1.87 mmol) with Ac_2O (385.0mg, 3.74 mmol) in pyridine as the method for **21** via column chromatography on silica gel (PE : EtOAc =50 : 1). ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.10 (d, *J* = 7.6 Hz, 2H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.52 (m, 2H), 7.48 (m, 4H), 7.38 (d, J_1 = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 5.26 (t, *J* = 10.0 Hz, 1H, H-4), 5.19 (dd, J_1 = 10.0 Hz, J_2 = 9.6 Hz, 1H, H-2), 4.84 (d, *J* = 9.6 Hz, 1H, H-1), 4.25 (m, 2H, H-6a, H-6b), 4.00 (dd, J_1 = 10.0 Hz, J_2 = 9.6 Hz, H-3), 3.91 (m, 1H, H-5), 2.35 (s, 3H,1-STol), 2.03 (s, 3H, 6-OAc). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 165.1, 165.1, 139.0, 134.0, 133.8, 130.2, 130.1, 129.9, 129.4, 128.9, 128.8, 128.8, 128.1, 86.9, 76.7, 70.9, 69.5, 66.4, 62.9, 21.4, 20.9. ESI-MS: calcd for $C_{29}H_{28}N_3O_7S$ $[M + H]^+$ 562.1570, found: 562.1688.

4.25. Synthesis of p-methylphenyl-3-azido-3-deoxy-2,4-di-O-benzoyl-6-O-benzyl-1-thio-β-D-glucopyranoside ***31b***

Ag_2O (1.3 g, 5.54 mmol) was added in a solution of compound **20** (957.0 mg, 1.84 mmol) in 7 mL DMF. Then BnBr (946.0 mg, 5.54 mmol) was added in and kept stirring for 10 hours. The reaction solution was filtered and filtrate was diluted with CH_2Cl_2, the diluent was washed with H_2O and the organic layer was concentrated and purified by column chromatography on silica gel(PE : EtOAc = 20 : 1) to give the compound **31b** (818.0 mg, 73%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.11 (d, *J* = 8.0 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 2H), 7.50 (m, 4H), 7.33 (m, 7H), 6.90 (d, *J* = 7.6 Hz, 2H), 5.07 (dd, J_1 = 10.0 Hz, J_2 = 9.6 Hz, H-4), 4.86 (d, *J* = 10.4 Hz, 1H, 6-OCH_2Ph), 4.73 (dd, J_1 = 10.4 Hz, J_2 = 9.2 Hz, H-2), 4.70 (d, *J* = 10.4 Hz, 1H, H-1), 4.64 (d, *J* = 10.4 Hz, 1H, 6-OCH_2Ph), 4.42 (dd, J_1 = 12.0 Hz, J_2 = 4.8 Hz, H-6a), 3.84 (dd, J_1 = 9.6 Hz, J_2 = 9.2 Hz, 1H), 3.74 (m, 1H), 3.60 (dd, J_1 = 10.0 Hz, J_2 = 9.2 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 166.2, 165.3, 138.7, 136.9, 134.2, 133.8, 133.5, 130.2, 130.0, 129.8, 128.8, 128.8, 128.7,

128.7, 128.6, 127.8, 86.3, 77.9, 76.4, 75.5, 70.9, 69.0, 63.3, 21.4. ESI-MS: calcd for $C_{34}H_{32}N_3O_6S$ $[M+H]^+$ 610.1934, found: 610.2010.

4.26. Synthesis of p-methylphenyl -3-azido-3-deoxy-2,4-di-O-benzoyl-6-O-methyl 1-thio-β-D-glucopyranoside ***31c***

Compound **31c** (727.8 mg, 70%) was obtained from compound **20** (1.0 g, 1.95 mmol) with MeI (830.7 mg, 5.85 mmol) and Ag_2O (1.4 g, 5.85 mmol) as the method for compound **31b** via column chromatography on silica gel (PE : EtOAc = 50 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.6 Hz, 2H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.62 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 4H), 7.32 (d, *J* = 7.6 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 5.02 (t, *J* = 10.0 Hz, 1H, H-4), 4.75 (dd, J_1 = 11.2 Hz, J_2 = 10.0 Hz, 1H, H-2), 4.72 (d, *J* = 10.0 Hz, 1H, H-1), 4.50 (dd, J_1 = 12.0 Hz, J_2 = 5.6 Hz, 1H, H-6a), 3.75 (m, 2H), 3.59 (s, 3H, 6-OMe), 3.31 (dd, J_1 = 10.0 Hz, J_2 = 9.2 Hz, 1H, H-3), 2.25 (s, 3H,1-STol). ^{13}C NMR($CDCl_3$, 100 MHz) δ 166.4, 165.3, 138.7, 134.1, 133.7, 133.5, 130.2, 130.0, 129.9, 129.8, 129.6, 128.8, 128.7, 127.8, 86.4, 79.0, 78.0, 77.6, 77.3, 76.9, 70.7, 68.5, 63.4, 61.1, 29.9, 21.4. ESI-MS: calcd for $C_{28}H_{28}N_3O_6S$ $[M+H]^+$ 534.1621, found: 534.1731.

4.27. Synthesis of 6-acetyl-3-azido-3-deoxy-2,4-di-O-benzoyl-D-glucopyranoside trichloroacetimidate ***33a***

Compound **33a** was obtained as the method for compound **27** in a yield of 58% for two steps. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.68 (s, 1H, -NH), 8.08 (d, *J* = 7.6 Hz, 2H), 8.03 (d, *J* = 7.6 Hz, 2H),7.61 (m, 2H), 7.46 (m, 4H), 6.71 (d, *J* = 3.2 Hz, 1H, H-1), 5.41 (t, *J* = 10.0 Hz, 1H, H-4), 5.34 (dd, J_1 = 10.8 Hz, J_2 = 2.8 Hz, 1H, H-2), 4.39 (t, *J* = 10.0 Hz, 1H, H-3), 4.36 (m, 1H, H-5), 4.23 (m, 2H), 2.03 (s, 3H, 6-OAc). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 165.4, 165.1, 160.5, 134.1, 134.1, 130.2, 130.2, 130.1, 128.9, 128.8, 128.7, 92.8, 71.3, 70.5, 68.6, 62.1, 61.8.

4.28. Synthesis of 3-azido-3-deoxy-2,4-di- O-benzoyl-6-O-benzyl-β-D-Glucopyranoside trichloroacetimidate ***33b***

Compound **32** (400.0 mg, 82%) was obtained from compound **31** (594.0 mg, 0.97 mmol) as the procedure for compound **22** via column chromatography on silica gel(PE : EtOAc =10 : 1) and was for next step directly. Compound **33** (350.0 mg, 77%) was formed from compound **32** (350.0 mg, 0.70 mmol) following the way for compound **27**. The crude product was purified by column chromatography on silica gel (Ethyl acetate : PE =1 : 20). ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.60 (s, 1H, C = NH), 8.07 (d, *J* = 8.0 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 2H), 7.48 (m, 4H), 7.37 (m, 4H), 7.28 (d, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 3.6 Hz, 1H, H-1), 5.27 (dd, J_1 = 10.0 Hz, J_2 = 3.6 Hz, H-2), 4.93 (d, *J* = 10.5 Hz, 1H, 6-OCH_2Ph), 4.68 (d, *J* = 10.5 Hz, 1H, 6-OCH_2Ph), 4.58 (m, 2H), 4.31 (m, 2H), 3.74 (dd, J_1 = 9.8 Hz, J_2 = 9.8 Hz, 1H, H-3). ^{13}C NMR($CDCl_3$, 100 MHz) δ 166.2, 165.6, 160.8, 136.8, 134.0, 133.5, 130.2, 130.0, 129.9, 128.9, 128.8, 128.7, 93.0, 75.8, 75.8, 71.8, 71.4, 64.3, 62.7.

4.29. Synthesis of 3-azido-3-deoxy-2,4-di-O-benzoyl-6-O-methyl-D-glucopyranoside trichloroacetimidate ***33c***

Compound **33c** was obtained as the method for compound **27** in a yield of 60% for two steps. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (s, 1H, -NH), 8.07 (d, *J* = 7.6 Hz, 4H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.47 (m, 4H), 6.10 (d, *J* = 3.2 Hz, 1H, H-1), 5.20 (dd, J_1 = 10.8 Hz, J_2 = 3.2 Hz, 1H, H-2), 4.62 (t, *J* = 11.2 Hz, 1H, H-4), 4.55 (m, 1H, H-6a), 4.20 (m, 2H), 3.64 (s, 3H, 6-OMe), 3.45 (t, *J* = 9.6 Hz, 1H, H-3). ^{13}C NMR($CDCl_3$, 100 MHz) δ 166.3, 165.5, 160.6, 133.9, 133.5, 130.2, 130.1, 129.9, 129.8, 128.9, 128.9, 128.8, 128.7, 93.0, 78.4, 77.6, 77.3, 77.0, 71.8, 71.1, 63.8, 62.8, 61.3, 27.1.

4.30. (E)-5-(6-O-acetyl-3-azido-3-deoxy-2,4-di-O-benzoyl-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***34a***

Compound **34a** (193.7 mg, 58%) was coupled by the donor **33a** (400.0 mg, 0.69 mmol) and the acceptor erythronolide (192.0 mg, 0.33 mmol) with the promoter TMSOTf (22.3 mg, 0.10 mmol) as the procedure for compound **28**. The crude product was purified by column chromatography on silica gel ($CHCl_3$: PE : MeOH = 250 : 250 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.03 (m, 6H), 7.61 (t, *J* = 7.6 Hz, 3H), 7.47 (m, 6H), 5.24 (t, *J* = 10.0 Hz, 2H, H-4′, H-2′), 5.08 (d, *J* = 9.2 Hz, 1H, H-13), 4.87 (s, 1H, H-11), 4.81 (d, *J* = 8.0 Hz, 1H, H-1′), 4.25 (m, 2H, H-6′), 4.21 (d, *J* = 5.2 Hz, 1H, H-2), 3.93 (m, 2H, H-3′, H-5′), 3.75 (m, 1H), 2.74 (s, 3H, 6-OMe), 1.94 (s, 3H, 6′-OAc), 1.33 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 170.6, 169.2, 165.2, 164.6, 163.8, 153.8, 134.1, 133.9, 133.4, 130.1, 130.0, 129.7, 129.5, 129.2, 128.9, 128.9, 128.8, 100.4, 77.5, 77.2, 72.9, 72.2, 69.8, 65.1, 62.6, 51.4, 50.1, 38.3, 28.6, 27.1, 22.8, 20.8, 19.9, 14.4, 13.6, 10.5. HRMS (ESI) $[M+H]^+$ 1013.3992, calcd for $C_{52}H_{61}N_4O_{17}$, 1013.3954.

4.31. (E)-5-(3-azido-3-deoxy-2,4-di- O-benzoyl-6- O-benzyl mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***34b***

Compound **34b** (82.9 mg, 46%) was coupled by the donor 33 (217.0 mg, 0.33 mmol) and the acceptor erythronolide (96.0 mg, 0.17 mmol) with the promoter TMSOTf (7.5 mg, 0.03 mmol) as the procedure for compound **28**. The crude product was purified by column chromatography on silica gel ($CHCl_3$: PE : MeOH = 500 : 500 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.01 (d, *J* = 7.7 Hz, 2H), 7.97 (d, *J* = 6.7 Hz, 4H), 7.50 (m, 7H), 7.30 (m, 7H), 5.11 (dd, J_1 = 9.2 Hz, J_2 = 9.0 Hz, H-2′), 5.04 (dd, J_1 = 10.1 Hz, J_2 = 2.8 Hz, H-13), 4.90 (d, *J* = 10.8 Hz, 1H, H-6′-OCH_2Ph), 4.81 (s, 1H, H-11), 4.71 (d, *J* = 8.0 Hz, H-1′), 4.66 (d, *J* = 10.8 Hz, 1H, H-6′-OCH_2Ph), 4.62 (d, *J* = 11.4 Hz, 1H, H-6′), 4.47 (dd, J_1 = 11.4 Hz, J_2 = 6.3 Hz, H-6′), 4.18 (d, *J* = 6.2 Hz, 1H, H-2), 3.84 (m, 1H), 3.80 (dd, J_1 = 9.8 Hz, J_2 = 9.2 Hz, 1H), 3.72 (m, 1H), 3.54 (dd, J_1 = 9.5 Hz, J_2 = 9.4 Hz, 1H), 2.93 (t, *J* = 7.2 Hz, 1H), 2.47 (s, 3H, H-6-OMe), 1.37 (d, J = 6.8 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H), 1.23 (s, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 7.6 Hz, 3H), 0.85 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.5, 169.2, 166.2, 164.9, 163.7, 153.8, 150.0, 136.9, 136.2, 133.8, 133.6, 133.3, 130.0, 129.8, 129.6, 129.3, 128.9, 128.8, 128.8, 128.7, 128.7, 124.0, 100.2, 78.0, 77.5, 77.0, 75.4, 74.2, 72.4, 67.6, 63.0, 51.3, 49.8, 38.1, 29.9, 28.6, 22.7, 19.9, 15.7, 14.4, 13.6, 10.5. HRMS (ESI) $[M+H]^+$ 1061.4366, calcd for $C_{57}H_{65}N_4O_{16}$, 1061.4317.

4.32. (E)-5-(3-azido-3-deoxy-2,4-di-O-benzoyl-6-O-methylmycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***34c***

Compound **34c** (254.3 mg, 68%) was coupled by the donor **33c** (452.0 mg, 0.75 mmol) and the acceptor erythronolide (227.0 mg, 0.38 mmol) with the promoter TMSOTf (16.7 mg, 0.07 mmol) as the procedure for compound **28**. The crude product was purified by column chromatography on silica gel ($CHCl_3$: PE : Methanol = 250 : 250 : 1). ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.00 (m, 6H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.46 (m, 4H), 7.38 (t, *J* = 7.6 Hz, 2H), 5.06 (dd, J_1 = 10.0 Hz, J_2 = 8.8 Hz, 2H, H-2′, H-13), 4.82 (s, 1H, H-11), 4.70 (d, *J* = 7.6 Hz, 1H, H-1′), 4.68 (t, *J* = 10.0 Hz, 1H, H-4′), 4.54 (dd, J_1 = 12.0 Hz, J_2 = 6.8 Hz, 1H, H-6a′), 4.20 (d, *J* = 6.0 Hz,

1H, H-2), 3.79 (m, 1H), 3.71 (m, 2H), 3.62 (s, 3H, 6′-OMe), 3.28 (t, J_1 = 9.6 Hz, 1H, H-3′), 2.94(m, 1H), 2.48 (s, 3H, 6-OMe), 1.38 (d, J = 6.4 Hz, 3H), 1.33 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 7.6 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H). HRMS (ESI) $[M+H]^+$ 985.4044, calcd for $C_{51}H_{61}N_4O_{16}$, 985.4004.

4.33. (E)-5-(6-O-acetyl-2,4-di-O-benzoyl- 3-dimethylamino-3-deoxy mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***35a***.

Compound **35a** was obtained as the method for compound **29** in a yield of 70% for two steps.^{1}H NMR($CDCl_3$, 400 MHz) δ 8.03 (m, 6H), 7.58 (t, J = 7.2 Hz, 3H), 7.51 (t, J = 7.2 Hz, 1H), 7.46 (m, 5H), 5.28 (t, J = 9.2 Hz, 2H, H-4′, H-2′), 5.08 (d, J = 8.8 Hz, 1H, H-13), 4.87 (s, 1H, H-11), 4.74 (d, J = 7.6 Hz, 1H, H-1′), 4.25 (d, J = 6.4 Hz, 1H, H-2), 4.21 (m, 2H, H-6′), 3.86 (m, 1H), 3.74 (m, 1H), 3.17 (t, J = 10.0 Hz, 1H, H-3′), 2.74 (s, 3H, 6-OMe), 2.34 (s, 6H, 3′-NMe_2), 1.94 (s, 3H, 6′-OAc), 1.33 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 7.2 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H). HRMS (ESI) $[M+H]^+$ 1015.4381, calcd for $C_{54}H_{67}N_2O_{17}$, 1015.4361.

4.34. (E)-5-(2,4- O-di-benzoyl-6- O-benzyl- 3-dimethylamino-3-deoxy mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***35b***

Compound **35b** (36.8 mg, 50%) was obtained from compound **34** (80.0 mg, 0.07 mmol) as the method for compound **29** via column chromatography on silica gel ($CHCl_3$: PE : MeOH= 500 : 500 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.03(m, 6H), 7.59 (dd, J_1 = 8.0 Hz, J_2 = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.44 (dd, J_1 = 8.0 Hz, J_2 = 7.6 Hz, 4H), 7.32 (m, 7H), 5.25 (dd, J_1 = 8.1 Hz, J_2 = 7.6 Hz, H-2’), 5.03 (dd, J_1 = 10.2 Hz, J_2 = 2.9 Hz, H-13), 4.92 (d, J = 10.7 Hz, 1H, H-6′-OCH_2Ph), 4.82 (s, 1H, H-11), 4.59-4.64 (m, 3H, H-1′, H-6′-OCH_2Ph, H-6′), 4.51 (dd, J_1 = 11.1 Hz, J_2 = 7.1 Hz, H-6′), 4.17 (d, J = 6.4 Hz, 1H, H-2), 3.82 (dd, J_1 = 8.7 Hz, J_2 = 7.5 Hz, 1H), 3.70 (dd, J_1 = 7.4 Hz, J_2 = 7.4 Hz, 2H), 3.48 (dd, J_1 = 9.6 Hz, J_2 = 9.5 Hz, 1H), 3.12 (dd, J_1 = 10.0 Hz, J_2 = 10.0 Hz, 1H), 2.90 (t, J = 7.3 Hz, 1H), 2.47 (s, 6H, H-3′- NMe_2), 2.39 (s, 3H, H-6-OMe), 1.37 (d, J = 6.7 Hz, 3H), 1.30 (d, J = 6.8 Hz, 3H), 1.23 (s, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.3, 169.2, 166.4, 164.9, 163.8, 153.9, 149.7, 138.1, 133.4, 133.3, 129.9, 129.7, 129.6, 128.8, 128.7, 128.7, 128.3, 128.2, 101.3, 82.2, 78.1, 77.4, 74.7, 74.6, 74.3, 70.9, 69.9, 64.0, 51.3, 49.7, 46.4, 41.7, 38.1, 31.8, 28.6, 27.1, 22.9, 20.0, 19.0, 15.7, 14.3, 13.5, 10.5. HRMS (ESI) $[M+H]^+$ 1063.4768, calcd for $C_{59}H_{71}N_2O_{16}$, 1063.4725.

4.35. (E)-5-(2,4-di-O-benzoyl-3-dimethylamino-3-deoxy-6-O-methyl mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxoerythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***35c***

Compound **35c** was obtained as the method for compound **29** in a yield of 71% for two steps. ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.00 (t, J_1 = 7.6 Hz, 6H), 7.57 (m, 2H), 7.46 (m, 5H), 7.37 (t, J_1 = 7.6 Hz, 2H), 5.18 (dd, J_1 = 9.6 Hz, J_2 = 8.8 Hz, 1H, H-2′), 5.04 (d, J = 9.6 Hz, 1H, H-13), 4.82 (s, 1H, H-11), 4.64 (m, 2H, H-4′, H-6b′), 4.57 (d, J = 7.2 Hz, 1H, H-1′), 4.19 (d, J = 6.0 Hz, 1H, H-2), 4.11 (dd, J_1 = 12.0 Hz, J_2 = 6.8 Hz, 1H, H-6a′),3.71 (m, 2H), 3.54 (s, 3H, 6′-OMe), 3.23 (t, J = 9.6 Hz, 1H, H-3′), 2.93(m, 2H), 2.44 (s, 6H, 3′-NMe_2), 2.42 (s, 3H, 6-OMe), 1.39 (d, J = 6.8 Hz, 3H), 1.32 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 7.6 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H). HRMS (ESI) $[M+H]^+$ 987.4437, calcd for $C_{53}H_{67}N_2O_{16}$, 987.4412.

4.36. (E)-5-(6-O- acetyl- 3-dimethylamino-3-deoxy mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***36a***

Compound **36a** was obtained as the method for compound **30** in a yield of 44%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.0 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 5.11 (d, J = 8.8 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.37 (d, J = 7.6 Hz, 1H, H-1′), 4.32 (m, 2H, H-6′), 4.25 (d, J = 6.8 Hz, 1H, H-2), 3.84 (m, 1H), 3.46 (m, 1H), 3.39 (m, 1H), 3.32 (t, J = 9.6 Hz, 1H), 3.06 (t, J = 10.0 Hz, 1H), 2.75 (s, 3H, 6-OMe), 2.51 (s, 6H, 3′-NMe_2), 2.03 (s, 3H, 6′-OAc), 1.44 (d, J = 6.8 Hz, 3H), 1.36 (d, J = 8.0 Hz, 3H), 1.35 (s, 3H), 0.90 (t, J = 7.6 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 203.9, 175.3, 171.4, 169.0, 163.6, 153.6, 133.2, 129.5, 129.3, 128.6, 103.3, 75.4, 70.5, 70.2, 66.1, 63.5, 51.2, 41.7, 38.5, 29.7, 28.6, 22.7, 20.8, 19.7, 14.5, 13.4, 10.4. HRMS (ESI) $[M+H]^+$ 807.3827, calcd for $C_{40}H_{59}N_2O_{15}$, 807.3837.

4.37. (E)-5-(6- O-benzyl- 3-dimethylamino-3-deoxy mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***36b***

Compound **36b** (15.6 mg, 62%) was yielded from the compound **35** (30.0 mg, 0.03 mmol) in methanol under refluxing condition. The crude product was purified by column chromatography on silica gel ($CHCl_3$: MeOH = 100 : 3). ^{1}H NMR($CDCl_3$, 600 MHz) δ 8.11 (dd, J_1 = 8.2 Hz, J_2 = 1.3 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.9 Hz, 2H), 7.36 (m, 5H), 5.07 (dd, J_1 = 10.2 Hz, J_2 = 2.7 Hz, H-13), 4.80 (s, 1H, H-11), 4.79 (d, J = 11.1 Hz, 1H, H-6′-OCH_2Ph), 4.70 (d, J = 11.8 Hz, 1H, H-6′), 4.62 (d, J = 11.1 Hz, 1H, H-6′-OCH_2Ph), 4.52 (dd, J_1 = 11.7 Hz, J_2 = 6.8 Hz, H-6′), 4.47 (d, J = 7.4 Hz, 1H, H-1′), 3.85 (m, 1H), 3.78 (m, 1H), 3.07 (t, J = 7.7 Hz, 1H), 2.60 (s, 6H, H-3′- NMe_2), 2.52 (s, 3H, H-6-OMe), 1.39 (d, J = 6.8 Hz, 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.4 Hz, 6H). ^{13}C NMR($CDCl_3$, 150 MHz) δ 203.9, 169.1, 166.2, 165.5, 154.0, 133.3, 129.8, 129.7, 128.6, 128.5, 128.1, 127.8, 103.1, 84.6, 82.9, 79.1, 78.1, 76.4, 75.0, 74.6, 73.4, 69.5, 63.5, 51.1, 49.6, 47.3, 38.1, 29.7, 25.2, 22.7, 22.4, 19.7, 18.7, 15.5, 15.4, 14.2, 14.1, 13.2, 10.3. HRMS (ESI) $[M+H]^+$ 855.4219, calcd for $C_{45}H_{63}N_2O_{14}$, 855.4201.

4.38. (E)-5-(3-dimethylamino-3-deoxy-6- O-methylmycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***36c***

Compound **36c** was obtained as the method for compound **30** in a yield of 35%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 7.80 (m, 4H), 7.55 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 5.07 (d, J = 9.2 Hz, 1H, H-13), 4.82 (s, 1H, H-11), 4.58 (d, J = 11.6 Hz, 1H, H-6b′), 4.51 (t, J = 11.2 Hz, 1H, H-4′), 4.43 (d, J = 7.2 Hz, 1H, H-1′), 4.20 (d, J = 6.0 Hz, 1H, H-2), 3.83 (m, 1H), 3.68 (m, 1H), 3.49 (s, 3H, 6′-OMe), 3.32 (t, J = 9.6 Hz, 1H), 3.20 (t, J = 8.4 Hz, 1H), 3.04(m, 1H), 2.52 (s, 6H, 3′-NMe_2), 2.44 (s, 3H, 6-OMe), 1.40 (d, J = 7.6 Hz, 3H), 1.35 (d, J = 6.4 Hz, 3H), 1.28 (d, J = 7.6 Hz, 3H), 1.08 (d, J = 6.0 Hz, 3H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.3, 175.4, 169.3, 166.4, 163.8, 153.9, 133.5, 133.3, 129.9, 129.7, 129.7, 129.5, 128.8, 128.7, 103.2, 82.1, 78.1, 75.2, 70.5, 69.6, 63.6, 59.2, 51.4, 49.9, 47.1, 41.8, 38.6, 29.9, 28.7, 22.8, 20.1, 19.1, 15.7, 14.4, 13.6, 10.6. HRMS (ESI) $[M+H]^+$ 779.3890, calcd for $C_{39}H_{59}N_2O_{14}$, 779.3888.

4.39. (E)-5-(3-dimethylamino-3-deoxy mycaminosy)-3-O-descla-

dinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***37a***

Compound **37a** was obtained as the method for compound **30** in a yield of 40%.^{1}H NMR($CDCl_3$, 400 MHz) δ 8.04 (d, J1 = 8.0 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 5.11 (d, *J* = 8.8 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.46 (d, *J* = 7.2 Hz, 1H, H-1′), 4.25 (d, *J* = 6.8 Hz, 1H, H-2), 3.86 (m, 2H, H-6′), 3.60 (t, *J* = 9.6 Hz, 1H), 3.40 (m, 2H), 3.07 (m, 1H), 2.76 (s, 3H, 6-OMe), 2.59 (s, 6H, 3′-NMe_2), 1.42 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.6 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR($CDCl_3$, 150 MHz) δ 175.3, 169.0, 163.6, 153.6, 133.2, 129.5, 129.2, 128.6, 103.2, 76.5, 70.5, 66.4, 62.8, 51.2, 50.2, 41.8, 31.9, 29.4, 22.7, 19.9, 14.5, 14.1, 13.4, 10.4. HRMS (ESI) $[M+H]^+$ 765.3730, calcd for $C_{38}H_{57}N_2O_{14}$, 765.3732.

4.40. (E)-5-(4-O-benzyol-3-dimethylamino-3-deoxy-6- O-methylmycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***37c***

Compound **37c** was obtained as the method for compound **30** in a yield of 40%. ^{1}H NMR($CDCl_3$, 500 MHz) δ 8.11 (d, J1 = 7.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 5.04 (d, *J* = 10.5 Hz, 1H, H-13), 4.79 (s, 1H, H-11), 4.67 (d, *J* = 11.5 Hz, 1H, H-6b′), 4.45 (dd, J_1 = 11.5 Hz, J_2 = 7.0 Hz, 1H, H-6a′), 4.43 (d, J = 8.0 Hz, 1H, H-1′), 4.24 (d, J = 8.0 Hz, 1H, H-2), 3.85 (m, 1H), 3.68 (m, 1H), 3.52 (s, 3H, 6'-OMe), 3.38 (t, J = 10.0 Hz, 1H), 3.25 (dd, J_1 = 10.5 Hz, J_2 = 7.5 Hz, 1H), 3.05(t, *J* = 7.5 Hz, 1H), 2.55 (s, 6H, 3′-NMe2), 2.51 (s, 3H, 6-OMe), 1.38 (d, *J* = 6.5 Hz, 3H), 1.35 (s, 3H), 1.25 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR($CDCl_3$, 125 MHz) δ 203.9, 169.1, 166.3, 165.3, 154.0, 133.3, 129.8, 129.7, 128.5, 103.1, 84.6, 82.9, 79.1, 78.1, 76.6, 76.3, 75.0, 70.3, 69.4, 63.6, 59.0, 51.1, 49.6, 47.3, 41.6, 38.1, 29.7, 22.4, 19.7, 18.7, 15.6, 15.4, 14.2, 13.1, 10.3. HRMS (ESI) [M+H]+ 793.4017, calcd for $C_{40}H_{61}N_2O_{14}$, 793.4045.

4.41. Synthesis of p-methylphenyl-3-azido-3-deoxy-4,6-O-benzylidene-1-thio-β-D-glucopyranoside ***38***

To a solution of compound **9** (1.5 g, 4.85 mmol) in 15 mL DMF were added in $PhCH(OMe)_2$ (1.5 g, 9.70 mmol) and PTSA (0.2 g, 0.73 mmol) at 50 ℃. After stirring for 5 hours, the reaction solution was added in Et_3N to neutralize and diluted with CH_2Cl_2, the diluent was washed with H_2O and saturated $NaHCO_3$. The organic phase was concentrated and purified by column chromatography on silica gel(PE : EtOAc = 20 : 1) to form compound **38** (1.3 g, 71%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 7.48 (m, 2H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.39 (m, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 5.55 (s, 1H), 4.55 (d, *J* = 9.6 Hz, 1H, H-1), 4.38 (dd, J_1 = 10.6 Hz, J_2 = 4.6 Hz, 1H, H-6), 3.76 (dd, J_1 = 10.6 Hz, J_2 = 9.9 Hz, 1H, H-6), 3.71 (dd, J_1 = 9.7 Hz, J_2 = 9.3 Hz, 1H, H-4), 3.54 (ddd, J_1 = 9.4 Hz, J_2 = 9.4 Hz, J_3 = 4.8 Hz, 1H, H-5), 3.47 (dd, J_1 = 9.5 Hz, J_2 = 9.4 Hz, 1H, H-3), 3.33 (ddd, J_1 = 9.4 Hz, J_2 = 9.4 Hz, J_3 = 2.4 Hz, 1H, H-2), 2.68 (d, *J* = 2.4 Hz, 1H, 2-OH), 2.37 (s, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 139.4, 136.9, 134.1, 130.2, 129.4, 128.6, 126.9, 126.2, 101.7, 89.4, 79.4, 71.8, 71.7, 68.8, 66.1, 21.4. ESI-MS: calcd for $C_{20}H_{22}N_3O_4S[M+H]^+$ 400.1253, found: 400.1268.

4.42. Synthesis of p-methylphenyl-3-azido-3-deoxy-2-O-benzoyl-4,6-O-ben-zylidene-1-thio-β-D-glucopyranoside ***39***

Compound **38** (0.8 g, 1.92 mmol) was dissolved in 5 mL pyridine, and BzCl (0.7 g, 0.14 mmol) was added in. After stirring for 2 hours, the reaction solution was concentrated and diluted with CH_2Cl_2, the diluent was washed with H_2O and saturated $NaHCO_3$. The organic phase was concentrated and purified by column chromatography on silica gel (PE : EtOAc = 40 : 1) to form compound **39** (1.3 g, 71%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.50 (m, 4H), 7.37 (m, 5H), 7.11 (d, *J* = 7.9 Hz, 2H), 5.61 (s, 1H), 5.12 (dd, J_1 = 9.7 Hz, J_2 = 9.7 Hz, 1H, H-2), 4.83 (d, *J* = 9.9 Hz, 1H, H-1), 4.44 (dd, J_1 = 10.7 Hz, J_2 = 4.8 Hz, 1H, H-6), 3.95 (dd, J_1 = 9.6 Hz, J_2 = 9.6 Hz, 1H, H-4), 3.83 (dd, J_1 = 10.2 Hz, J_2 = 10.1 Hz, 1H, H-6), 3.68 (dd, J_1 = 9.6 Hz, J_2 = 9.3 Hz, 1H, H-3), 3.60 (m, 1H, H-5), 2.34 (s, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 165.1, 139.0, 136.8, 134.0, 133.8, 130.2, 130.0, 129.5, 129.4, 128.8, 128.6, 128.0, 126.2, 101.7, 87.6, 79.5, 71.6, 71.1, 68.8, 65.0, 21.4. ESI-MS: calcd for $C_{27}H_{26}N_3O_5S$ $[M+H]^+$ 504.1515, found: 504.1589.

4.43. Synthesis of 3-azido-3-deoxy-2-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside trichloroacetimidate ***41***

Compound **39** (0.2 g, 0.42 mmol) was dissolved in a mixture solution of 3 mL CH_2Cl_2 and 0.3 mL H_2O and NIS (98.0 mg, 0.42 mmol) was added in. After stirring for 10 minutes, TFA (45.0 mg, 0.42 mmol) was added in and kept stirring for 5 hours. The reaction solution was washed with saturated $NaHCO_3$ solution and $Na_2S_2O_3$ solution. The organic layer was concentrated and purified by column chromatography on silica gel(PE : EtOAc = 20 : 1) to form compound **40** (90.0 mg, 55%). Compound **41** (262.0 mg, 96%) was obtained from compound **40** (200.0 g, 0.50 mmol) as the procedure for compound **27**. The crude product was purified by column chromatography on silica gel (PE : EtOAc = 40 : 1) to form compound **41** (262.0 mg, 96%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.61 (s, 1H, C = NH), 8.05 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 6.8 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 6.6 Hz, 3H), 6.62 (d, *J* = 3.7 Hz, 1H, H-1), 5.66 (s, 1H), 5.22 (dd, J_1 = 10.3 Hz, J_2 = 3.7 Hz, 1H, H-2), 4.41 (dd, J_1 = 10.6 Hz, J_2 = 4.9 Hz, 1H, H-6), 4.36 (dd, J_1 = 10.2 Hz, J_2 = 9.0 Hz, 1H), 3.83 (dd, J_1 = 10.6 Hz, J_2 = 10.4 Hz, 3H).

4.44. (E)-5-(3-azido-3-deoxy-2- O-benzoyl-4,6-O-benzylidenemycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate ***42***

Compound **42** (140.0 mg, 60%) was coupled by the donor **41** (270.0 mg, 0.50 mmol) and the acceptor erythronolide (140.0 mg, 0.25 mmol) with the promoter TMSOTf (13.9 mg, 0.06 mmol) as the procedure for compound **28**. The crude product was purified by column chromatography on silica gel ($CHCl_3$: PE : MeOH= 500 : 500 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.03 (m, 4H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.49 (m, 6H), 7.38 (m, 3H), 5.61 (s, 1H), 5.12 (dd, J_1 = 8.8 Hz, J_2 = 8.9 Hz, 1H, H-2′), 5.08 (dd, J_1 = 10.1 Hz, J_2 = 2.7 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.79 (d, *J* = 7.9 Hz, 1H, H-1′), 4.43 (dd, J_1 = 10.6 Hz, J_2 = 4.8 Hz, 1H, H-6′), 4.24 (d, *J* = 6.5 Hz, 1H, H-2), 3.90 (dd, J_1 = 9.8 Hz, J_2 = 9.7 Hz, 1H), 3.79 (dd, J_1 = 10.2 Hz, J_2 = 10.1 Hz, 1H), 3.68 (dd, J_1 = 9.6 Hz, J_2 = 8.8 Hz, 1H), 3.61 (m, 1H, H-5′), 2.97 (t, *J* = 7.2 Hz, 1H), 2.74 (s, 3H, 6-OMe), 1.14 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 7.7 Hz, 3H), 0.86 (t, J = 7.6 Hz, 6H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.5, 175.3, 169.2, 164.8, 163.7, 153.9, 136.8, 133.9, 133.4, 130.1, 129.7, 129.4, 129.2, 128.9, 128.8, 128.5, 126.2, 101.8, 100.7, 79.8, 78.1, 77.1, 72.7, 68.7, 76.3, 63.6, 51.3, 50.2, 46.4, 38.2, 29.9, 28.6, 27.4, 22.7, 20.0, 19.0, 15.8, 14.9, 14.4, 13.6, 10.5. HRMS (ESI) $[M+H]^+$ 955.3962, calcd for $C_{50}H_{59}N_4O_{15}$, 955.3899.

4.45. (E)-5-(2-O-benzoyl-4,6-O-benzylidene-3-dimethylamino-3-deoxy-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-eryth-

*ronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **43***

Compound **43** (12.0 mg, 60%) was obtained from compound **42** (20.0 mg, 0.02 mmol) as the method for compound **29** via column chromatography on silica gel ($CHCl_3$: PE : MeOH= 500 : 500 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.04 (d, *J* = 7.6 Hz, 2H), 8.00 (d, *J* = 7.9 Hz, 2H), 7.59 (m, 2H), 7.50 (m, 7H), 7.36 (m, 2H), 5.55 (s, 1H), 5.08 (m, 2H, H-2′, H-13), 4.85 (s, 1H, H-11), 4.75 (d, *J* = 7.7 Hz, 1H, H-1′), 4.40 (dd, J_1 = 10.5 Hz, J_2 = 4.7 Hz, 1H, H-6′), 4.24 (d, *J* = 7.0 Hz, 1H, H-2), 3.71-3.82 (m, 3H), 2.74 (s, 3H, 6-OMe), 2.46 (s, 6H, H-3′-NMe_2), 1.36 (s, 3H), 1.32 (d, *J* = 6.7 Hz, 6H), 0.97 (d, *J* = 7.9 Hz, 3H). HRMS (ESI) $[M+H]^+$ 957.4362, calcd for $C_{52}H_{65}N_2O_{15}$, 957.4307.

*4.46. (E)-5-(4,6-O-benzylidene-3-dimethylamino-3-deoxymycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **44***

Compound **44** (7.0 mg, 65%) was yielded from the compound **43** (12.0 mg, 0.01 mmol) in methanol at room temperature for 12 hours. The crude product was purified by column chromatography on silica gel ($CHCl_3$: MeOH = 100 : 3). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.05 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (m, 4H), 7.37 (m, 3H), 5.51 (s, 1H), 5.09 (d, *J* = 10.1 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.52 (d, *J* = 7.4 Hz, 1H, H-1′), 4.33 (dd, J_1 = 10.4 Hz, J_2 = 4.8 Hz, 1H, H-6′), 4.25 (d, *J* = 7.6 Hz, 1H, H-2), 3.86 (m, 1H), 3.72 (dd, J_1 = 10.0 Hz, J_2 = 9.8 Hz, 2H), 3.47 (m, 1H, H-5′), 3.26 (t, *J* = 8.8 Hz, 1H), 3.08 (t, *J* = 7.6 Hz, 1H), 2.76 (s, 3H, 6-OMe), 2.53 (s, 6H, H-3′-NMe_2), 1.43 (d, *J* = 7.0 Hz, 6H), 1.37 (d, *J* = 6.9 Hz, 6H),1.32 (d, *J* = 7.4 Hz, 6H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.91 (t, *J* = 7.9 Hz, 3H). ^{13}C NMR($CDCl_3$, 100 MHz) δ 204.0, 169.0, 163.6, 163.6, 153.7, 137.2, 133.1, 129.5, 129.4, 129.0, 128.6, 128.3, 125.9, 103.6, 100.9, 69.9, 68.9, 68.2, 67.8, 51.2, 50.2, 41.7, 29.7, 28.6, 19.8, 14.3, 13.4, 10.4. HRMS (ESI) $[M+H]^+$ 853.4089, calcd for $C_{45}H_{61}N_2O_{14}$, 853.4045.

*4.47. Synthesis of p-methylphenyl-3-azido-3-deoxy-2-O-benzoyl-6-O-benzyl-1-thio-β-D-glucopyranoside **45***

Compound **39** was dissolved in 20 mL CH_2Cl_2 at ice-bath. Then Et_3SiH (2.1 g, 1.77 mmol) and TFA（2.0 g，1.77 mmol） were added and stirred at room temperature for 10 hours. After that, the solution was neutralized by saturated $NaHCO_3$ and washed by brine. Then the organic phase was concentrated and purified by column chromatography on silica gel (PE : EtOAc = 50: 1) to form compound **45** (1.0 g, 56%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.34 (m, 6H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.07 (t, *J* = 9.2 Hz, 1H, H-2), 4.76 (d, *J* = 10.0 Hz, 1H, H-1), 4.60, 4.56 (d, *J* = 12.0 Hz, 2H, 6-OBn, AB), 3.85 (dd, J_1 = 10.0 Hz, J_2 = 4.8 Hz, 1H), 3.78 (J_1 = 11.2 Hz, J_2 = 4.8 Hz, 1H), 3.70 (m, 2H), 3.60 (m, 1H), 2.30 (s, 3H, 1-STol). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3, 138.7, 137.6, 133.7, 130.2, 129.9, 129.6, 128.7, 128.1, 87.0, 78.5, 74.1, 71.6, 70.9, 70.6, 68.6, 21.4. ESI-MS $[M+Na]^+$ 528.1671, calcd for $C_{27}H_{27}N_3O_5SNa$, 528.1562.

*4.48. Synthesis of p-methylphenyl-3-azido-3-deoxy-2-O-benzoyl-4,6-di-O-benzyl -1-thio-β-D-glucopyranoside **46a***

Compound **45** (430.0 mg, 0.85 mmol) was dissolved in 5 mL DMF and NaH (60.0 mg, 1.49 mmol) at ice-bath. After stirring for 10 minutes, 0.1 mL BnBr was added and kept stirring for 12 hours at room temperature. Then the solution was quenched by methanol and diluted by CH_2Cl_2, the diluent was washed by brine and the organic layer was concentrated. The crude product was purified by column chromatography on silica gel (PE : EtOAc = 50 : 1) to form compound **46a** (500.0mg, 99%). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 3H), 7.33 (m, 11H), 7.04 (d, *J* = 8.0 Hz, 2H), 5.08 (t, *J* = 9.6 Hz, 1H, H-2), 4.81, 4.73 (d, *J* = 11.4 Hz, 2H, 6-OBn, AB), 4.62 (m, 3H), 3.78 (m, 3H), 3.62 (t, *J* = 9.2 Hz, 1H), 3.58 (t, J = 9.2 Hz, 1H), 2.30 (s, 3H, 1-STol).

*4.49. Synthesis of p-methylphenyl-3-azido-3-deoxy-2-O-benzoyl-6-O-benzyl-4-O-methyl-1-thio-β-D-glucopyranoside **46b***

Compound **46b** (513.0 mg, 99%) was obtained from compound **45** (500.0mg, 0.99mmol) as the procedure for compound **46a** via column chromatography on silica gel (PE : EtOAc = 50 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.48 (m, 3H), 7.36 (m, 6H), 7.01 (d, *J* = 8.0 Hz, 2H), 5.02 (t, *J* = 10.0 Hz, 1H, H-2), 4.70 (d, *J* = 9.6 Hz, 1H, H-1), 4.63 (d, *J* = 12.8 Hz, 2H, 6-OBn, AB), 3.75 (m, 4H), 3.54 (s, 3H, 4-OMe), 3.33 (m, 1H), 2.29 (s, 3H, 1-STol).

*4.50. Synthesis of 3-azido-3-deoxy-2-O-benzoyl-4,6-di-O-benzyl-α-D-glucopyranoside trichloroacetimidate **47a***

Compound **47a** (113.0 mg, 53%) was formed from compound **46a** (130.0 mg，0.27 mmol) following the way for compound **41**. The crude product was purified by column chromatography on silica gel (PE : EtOAc = 40 : 1). ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.54 (s, 1H, 1-NH), 8.04 (d, *J*= 7.6 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.32 (m, 8H), 6.63 (d, *J* = 2.8 Hz, 1H, H-1), 5.18 (t, J_1 = 10.4 Hz, J_2 = 3.2 Hz 1H, H-2), 4.83, 4.54 (d, *J* = 11.4 Hz, 2H, 6-OBn, AB), 4.66, 4.60 (d, *J* = 11.6 Hz, 2H, 6-OBn, AB), 4.21 (t, *J* = 10.4 Hz, 1H), 4.04 (d, *J* = 9.6 Hz, 1H), 3.84 (m, 2H), 3.70 (d, *J* = 10.8 Hz, 1H).

*4.51. (E)-5-(3-azido-3-deoxy-2-O-benzoyl-4,6-di-O-benzylmycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **48a***

Compound **48a** was obtained as the method for compound **28** in a yield of 70%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 7.6 Hz, 3H), 8.02 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.44 (m, 4H), 7.33 (m, 5H), 7.26 (m, 3H), 5.10 (dd, J_1 = 11.6 Hz, J_2 = 8.0 Hz, 1H, H-2'), 5.05 (d, *J* = 10.8 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.80 (d, *J* = 11.4 Hz, 1H, 6′-OBn), 4.62 (d, *J* = 9.2 Hz, 2H, 6′-OBn, H-1′), 4.53 (s, 2H, 4′-OBn), 4.20 (d, *J* = 6.8 Hz, 1H, H-2), 3.72 (m, 5H), 3.54 (m, 1H), 2.94 (t, *J*= 7.6 Hz, 1H), 2.68 (s, 3H, 6-OMe), 1.32 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 5.6 Hz, 3H), 0.94 (d, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 1H). HRMS (ESI) $[M+H]^+$ 1047.4564, calcd for $C_{57}H_{67}N_4O_{15}$, 1047.4525.

*4.52. (E)-5-(3-azido-3-deoxy-2-O-benzoyl-6-O-benzyl-4-O-methyl-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **48b***

Compound **48b** was obtained as the method for compound **28** in a yield of 62%.^{1}H NMR($CDCl_3$, 400 MHz) δ 8.05 (d, J_1 = 7.6 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.53 (m, 1H), 7.46 (m, 4H), 7.23 (m, 4H), 5.05 (m, 2H, H-2, H-13), 4.86 (s, 1H, H-11), 4.62 (d, *J* = 8.0 Hz, 1H, H-1′), 4.56 (s, 2H, 6'-OBn), 4.30 (t, *J* = 6.8 Hz, 1H), 4.20 (d, *J* = 6.8 Hz, 1H, H-2), 3.73 (m, 3H), 3.61 (t, *J* = 9.6 Hz, 2H), 3.56 (s, 3H, 4′-OMe), 3.45 (m, 2H), 2.68 (s, 3H, 6-OMe), 1.32 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 7.6 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H). HRMS (ESI) $[M+H]^+$ 971.4252 calcd for $C_{51}H_{63}N_4O_{15}$, 971.4212.

4.53. (E)-5-(2-O-benzoyl-4,6-di-O-benzyl-3-dimethylamino-3-deoxy-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-ery-

*thronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **49a***

Compound **49a** was obtained as the method for compound **29** in a yield of 70%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 7.6 Hz, 3H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.44 (m, 4H), 7.28 (m, 8H), 5.24 (dd, J_1 = 9.2 Hz, J_2 = 8.8 Hz, 1H, H-2′), 5.05 (d, *J* = 9.6 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.84 (d, *J* = 11.6 Hz, 1H, 6′-OBn), 4.56 (m, 2H, 6′-OBn, H-1′), 4.54 (s, 2H, 4′-OBn), 4.18 (d, *J* = 6.8 Hz, 1H, H-2), 3.70 (m, 4H), 3.49 (m, 1H), 2.68 (s, 3H, 6-OMe), 2.44 (s, 6H, 3′-NMe_2), 1.31 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 7.6 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 1H). HRMS (ESI) $[M+H]^+$ 1049.4957 calcd for $C_{59}H_{73}N_2O_{15}$, 1049.4933.

4.54. (E)-5-(2-O-benzoyl-6-di-O-benzyl-3-dimethylamino-3-deo-

*xy-4-O-methyl-mycaminosy)-3-O-descladinosyl-6-O-methyl-3-o-xo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **49b***

Compound **49b** was obtained as the method for compound **29** in a yield of 65%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.42 (m, 3H), 7.22 (m, 3H), 5.17 (dd, J_1 = 9.6 Hz, J_2 = 8.8 Hz, 1H, H-2′), 5.05 (d, *J* = 8.4 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.56 (s, 2H, 6′-OBn), 4.54 (d, *J* = 8.8 Hz, 1H, H-1′), 4.19 (d, *J* = 7.2 Hz, 1H, H-2), 3.67 (m, 3H), 3.48 (s, 3H, 4′-OMe), 2.67 (s, 3H, 6-OMe), 2.42 (s, 6H, 3′-NMe_2), 1.31 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 7.6 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H). HRMS (ESI) $[M+H]^+$ 973.4632 calcd for $C_{53}H_{69}N_2O_{15}$, 973.4620.

4.55. (E)-5-(4,6-di-O-benzyl-3-dimethylamino-3-deoxy-mycami-

*nosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **50a***

Compound **50a** was obtained as the method for compound **30** in a yield of 55%.^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.31 (m, 3H), 7.23 (m, 7H), 5.08 (d, *J* = 10.0 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.68 (d, *J* = 11.8 Hz, 1H, 6′-OBn), 4.56 (m, 3H, 6′-OBn, 4′-OBn), 4.37 (d, *J* = 7.2 Hz, H-1′), 4.22 (d, *J* = 8.0 Hz, 1H, H-2), 3.81 (m, 2H), 3.66 (m, 2H), 3.40 (d, *J* = 8.8 Hz, 1H), 3.26 (dd, *J* = 10.0 Hz, *J* = 7.6 Hz, 1H), 3.06 (t, *J* = 7.6 Hz, 1H), 2.73 (s, 3H, 6-OMe), 2.51 (s, 6H, 3′-NMe_2), 1.35 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 5.6 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.1, 175.6, 169.2, 163.8, 153.9, 138.0, 137.8, 133.3, 129.7, 128.8, 128.7, 128.6, 128.1, 128.1, 128.0, 103.7, 76.9, 76.6, 73.8, 73.5, 73.1, 70.9, 69.7, 68.5, 51.4, 50.3, 41.9, 29.9, 28.8, 22.8, 20.2, 15.8, 15.7, 14.5, 13.6, 10.6. HRMS (ESI) $[M+H]^+$ m/z 945.4683 calcd for $C_{52}H_{69}N_2O_{14}$, 945.4671.

4.56. (E)-5-(6-O-benzyl-3-dimethylamino-3-deoxy-4-O-methylm-

*ycaminosy)-3-O-descladinosyl-6-O-methyl-3-oxo-erythronolide A 9-O-(benzoyl) oxime 11,12-cyclic carbonate **50b***

Compound **50b** was obtained as the method for compound **30** in a yield of 69%. ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.24 (m, 5H), 5.10 (d, *J* = 8.0 Hz, 1H, H-13), 4.86 (s, 1H, H-11), 4.56, 4.52 (d, *J* = 12.0 Hz, 1H, 6′-OBn), 4.33 (d, *J* = 7.6 Hz, 1H, H-1′), 4.20 (d, *J* = 7.6 Hz, 1H, H-2), 3.85 (m, 1H), 3.64 (m, 2H), 3.53 (t, *J* = 9.6 Hz, 1H), 3.43 (s, 3H, 4′-OMe), 3.30 (d, *J* = 8.8 Hz,1H), 3.20 (d, *J* = 8.0 Hz, 1H), 2.71 (s, 3H, 6-OMe), 2.49 (s, 6H, 3′-NMe_2), 1.36 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 6.4 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.1, 175.6, 169.2, 163.8, 154.0, 137.9, 133.3, 129.7, 129.6, 128.8, 128.6, 128.0, 128.0, 103.7, 76.8, 76.6, 75.4, 73.7, 70.8, 69.6, 68.5, 58.9, 51.4, 50.3, 47.6, 41.9, 38.7, 29.9, 28.8, 22.7, 20.2, 14.5, 13.6, 10.6. HRMS (ESI) $[M+H]^+$ 869.4372 calcd for $C_{46}H_{65}N_2O_{14}$, 869.4358.

Acknowledgements

This work was supported by the National S&T Major Special Project on Major New Drug innovation (Item Number: 2014ZX09507-009-09 and 2009ZX09301-003) and National Natural Science Foundation of China (81072524). And we are grateful to the Department of Instrumental Analysis of our institute for performing the NMR and mass spectroscopy measurements.

Supplementary date

Supplementary date associated with this article can be found in the online version.

References and notes

1. (a) Takashima, H. Curr. Top. Med. Chem. 2003, 3, 991. (b) Pfister, P.; Jenni, S.; Poehlsgaard, J.; Thomas, A.; Douthwaite, S.; Ban, N.; Bottger, E. C. J. Mol. Biol. 2004, 342, 1569. (c) Hansen, J. L.; Ippolito, J. A.; Ban, N.; Nissen, P.; Moore, P.; Steitz, T. A. Mol. Cell. 2002, 10, 117. (d) Poulsen, S. M.; Kofoed, C.; Vester, B. J. Mol. Biol. 2002, 34, 471. (e) Zuckerman, J. M.; Qamar, F.; Bono, B. R.; Medical Clinics of North America. 2011, 95, 761.
2. (a) N. LeTourneau.; P. Vimal.; D. Klepacki.; A. Mankin.; A. Melman. Bioorg. Med. Chem. Lett. 2012 , 4575-4578. (b) Audun, H; Kjell, Undheim. Bioorganic & Medicinal Chemistry. 2007, 15: 3266-3277. (c) Randolph, J. T.; Sauer, D. R.; Haviv, F.; Nilius, A. M.; Greer, J. Bioorg. Med. Chem. Lett. 2004, 14, 1599. (d) Mereu, A.; Moriggi, E.; Napoletano, M.; Regazzoni, C.; Manfredini, S.; Mercurio, T. P.; Pellacini, F. Bioorg. Med. Chem. Lett. 2006, 16, 5801.
3. Ly T, Phan.; Tianying, Jian.; Zhigang, Chen.; Yanling, Qiu.; Zhaolin, Wang.; Thersesa, B.; Alex, P.; Yat Sun, Qr. J. Med, Chem. 2004, 47, 2965.
4. (a) Chen, X.; Xu, P.; Xu, Y.; Liu, L.; Liu, Y.; Zhu, D.; Lei, P. Bioorg. Med. Chem. Lett. 2012, 22, 7402. (b) Xu, Y.; Chen, X.; Zhu, D.; Liu, Y.; Zhao, Z.; Jin, L.; Liu, C.; Lei, P. Eur. J. Med. Chem. 2013, 69, 174. (c) Chen, X.; Xu, Y.; Zhao, Z.; Lei, P. Tetrahedron Letters. 2014, 55, 6128-6130.
5. Romero, A.; Liang, C.-H.; Chiu, Y.-H.; Yao, S.; Duffield, J.; Sucheck, S. J.; Marby, K.; Rabuka, D.; Leung, P. Y.; Shue, Y.-K.; Ichikawa, Y.; Hwang, C.-K. Tetrahedron Lett. 2005, 46, 1483-1487.
6. Liang, C.-H.; Yao, S.; Chiu, Y.-H.; Leung, P. Y.; Robert, N.; Seddon, J.; Sears, P.; Hwang, C.-K.; Ichikawa, Y.; Romero, A. Bioorg. Med. Chem. Lett. 2005, 15,1307-1310.
7. Signe, M. C.; Henrik, F. H.; Troels, K. Organic Process Research & Development. 2004, 8, 777-780.
8. Milton, J. K.; Birgit, B.; Simon, B.; Ian, D. H.; Mark, V. I. J. Med. Chem. 1996, 39, 1314-1320.
9. Saito, Y.; Zevaco, T. A.; Agrofoglio, L. A. Tetrahedron. 2002, 124, 10642-10643.
10. Shazia, A.; Natasha, D. V.; Joseph, E. R.; David, R. J. P. Tetrahedron. 2013, 69, 816-825
11. Hansen, S. U.; Miller, G. J.; Barath, M.; Broberg, K. R.; Avizienyte, E.; Helliwell, M.; Raftey, J.; Jayson, G. C.; Gardiner, J. M. J. Org. Chem. 2012, 77, 7823-7843.
12. David, C.; Xu, H. J. Org. Chem. 2007, 72, 5183-5192.
13. Yu, G.; Gololobov, I. N.; Zhmurova, L. F.; Kasukhin. Tetrahedron. 1981, 37, 437-472.
14. Mcwilliams, J. C.; Clardy, J. J. Am. Chem. Soc. 1994, 116, 8378.

15. (a) Mohammad, M.; Meiliana, T.; Jun, Q. J. Am. Chem. Soc. 2007, 131, 9648-9650. (b) . Jui, T. B. K.; Ka, W, C.; Geoffrey, M. W.; Kerstin, M.; Bernadett, B.; John, A. R.; Margaret, A. B. Chemistry - A European Journal, 2003, 19, 12. (c) Peter, W.; Chen, B. W. Org. Lett. 2006, 8, 2381-2384.
16. (a) Samuel, D.; Joung, Y. L.; J. Am. Chem. Soc. 1989, 111, 4829-4813. (b) John, S. D.; Robert, R.; Bert, F. R. J. Org. Chem. 1997, 62, 4591-4600.
17. Zhang, J.; Sun, Y.; Zhang, X.; Li, C.; Guan, H. Carbohydrate Research. 2013, 381, 74-82.
18. (a) Shi, W.; Todd, L. L. Bioorg. Med. Chem. Lett. 2011, 21,2591-2596. (b) Joel, A. B.; Karrune, W.; Patricio, P. V.; Alejandro, V.; Educordo, M. S.; Alan, P. K. J. Med. Chem. 2012, 55, 2599-2605. (c) Sanjeev, K.; Masilamani, E. S.; Uma, R. Tetrahedron: Asymmetry. 2005, 16, 2599-2605
19. Mercedes, D.; Julio, D. M. J. Org. Chem. 1999, 64, 4798-4810.
20. Carrillo, R.; Morales, E. Q.; Martin, V. S.; Martin, T. Chemistry-A European Journal. 2013, 19, 7042.
21. (a) Surendra, K.; Srilakshmi, N.; Krish, N.; Pavan, K.; Sridhar, K.; Ramarao, K. Tetrahedron Lett. 2005, 46, 4581. (b) Loevyova, Z.; Parkan, K.; Kaiezo, L. Tetrahedron. 2011, 67, 4967.
22. Paul, S.; Raghothama, S.; Jayaraman, N. Carbohydrate Research. 2009, 344, 177.
23. Masahiro, W.; Rumi, O.; Kento, M.; Yuhei, K.; Tako, K.; Chiho, S.; Yasuo, S. Bioorg. Med. Chem. Lett. 2015, 25,1407-1411.