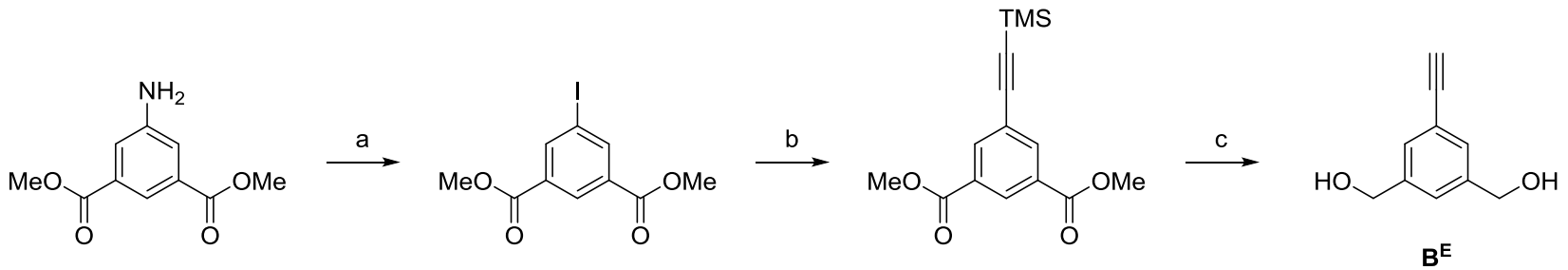
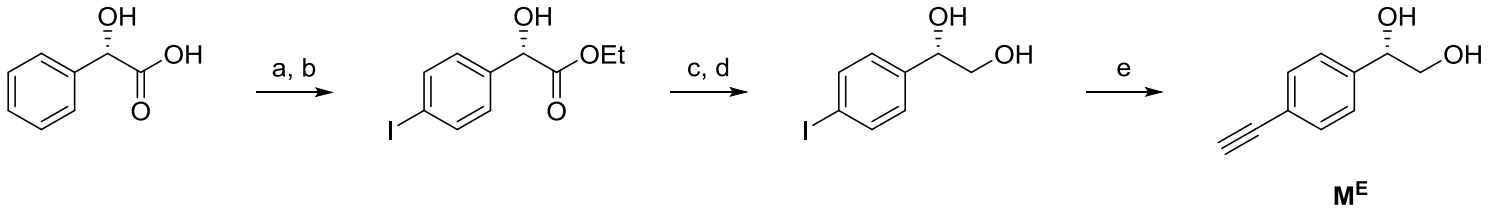
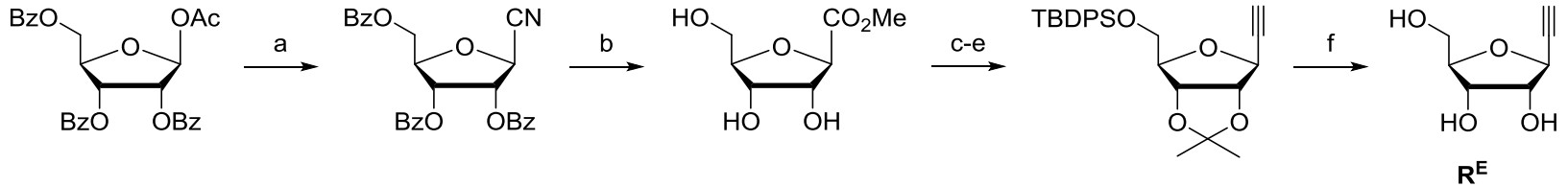
Practical and reliable synthesis of nucleic acid mimics containing ethynyl groups



Synthesis of **B**^{E}. Reagents and conditions: (a) i) HCl, $NaNO_2$, H_2O, 0 ºC; ii) KI, H_2O, 0 ºC, then rt, 55% (two steps); (b) TMS-acetylene, $PdCl_2(PPh_3)_2$, CuI, PPh_3, piperidine, THF, rt, 95%; (c) $LiAlH_4$, THF, 60 ºC, 70%.

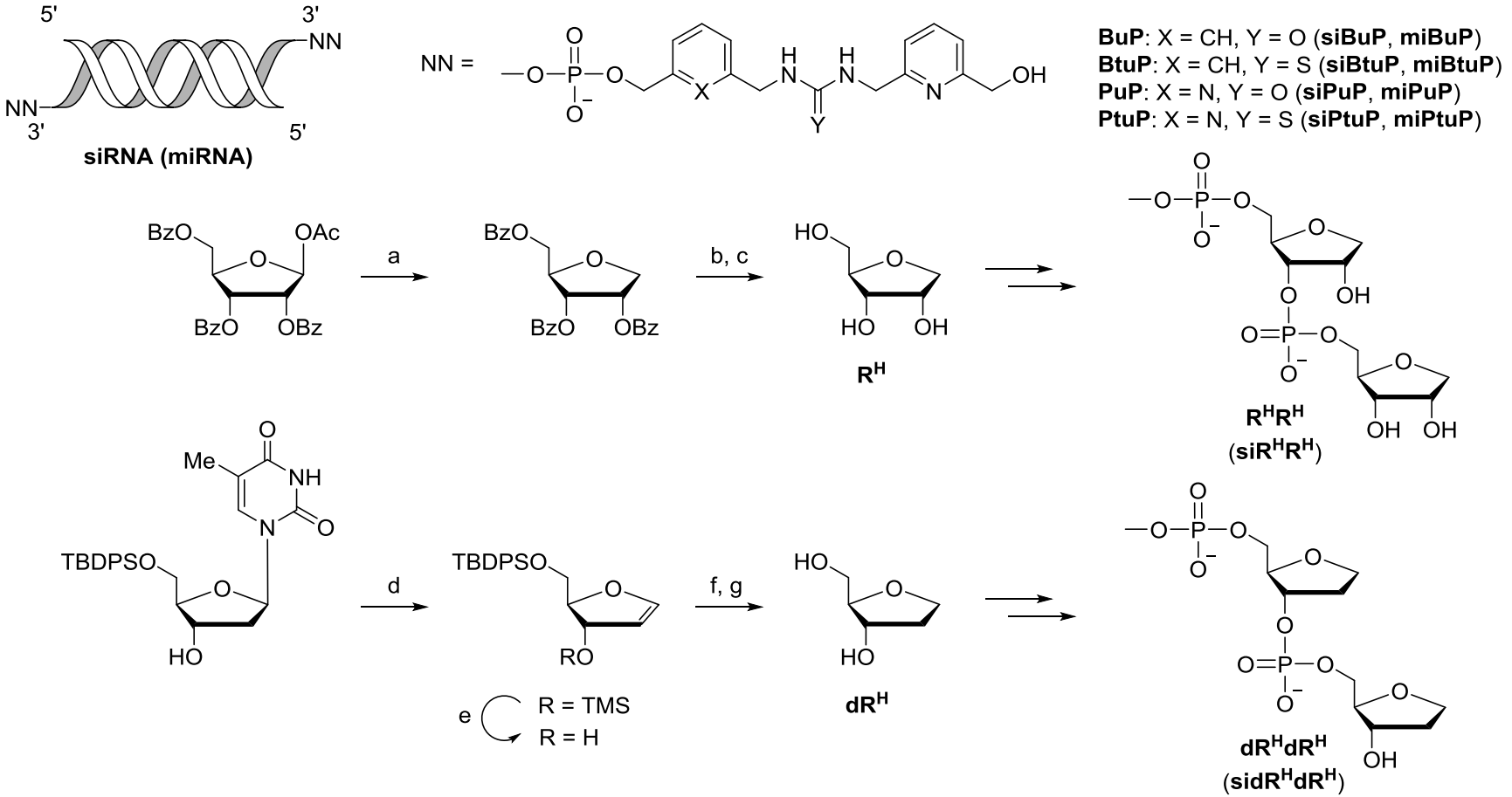


Synthesis of **M**^{E}. Reagents and conditions: (a) H_2SO_4, EtOH, 70 ºC, 97%; (b) I_2, AgOTf, CH_2Cl_2, rt, 68%; (c) $NaBH_4$, EtOH, rt, 86%; (d) TMS-acetylene, $PdCl_2(PPh_3)_2$, CuI, piperidine, rt, 85%; (e) K_2CO_3, MeOH, H_2O, rt, quant.



Synthesis of **R**^{E}. Reagents and conditions: (a) TMSCN, TMSOTf, CH_2Cl_2, rt, quant; (b) (i) NaOMe, MeOH, rt; (ii) HCl, rt, 70%; (c) TBDPSCl, pyridine, rt, 79%; (d) 2,2-dimethoxypropane, *p*-TsOH, acetone, 94%; (e) i) DIBAL-H, CH_2Cl_2, -78 ºC; ii) Bestmann-Ohira reagent, K_2CO_3, MeOH, rt, 67%; (f) CF_3CO_2H, H_2O, rt, 79%.

Design and synthesis of chemically modified functional RNAs bearing nucleic acid mimics at their 3′-overhang region which plays a key role in RNAi



Synthesis of **R^H** & **dR^H**. Reagents and conditions: (a) Et_3SiH, TMSOTf, MeCN, rt, quant; (b) i) NaH, MeOH, rt; ii) BnBr, NaH, DMF, rt, quant; (c) H_2, $Pd(OH)_2/C$, MeOH, rt, 94%; (d) $(NH_4)_2SO_4$, HMDS, reflux; (e) K_2CO_3, MeOH, rt; (f) H_2, Pd/C, *i*-PrOH, rt, 94%; (g) TBAF, THF, rt, 97%.

Practical Platform for Synthesis of Macrolides

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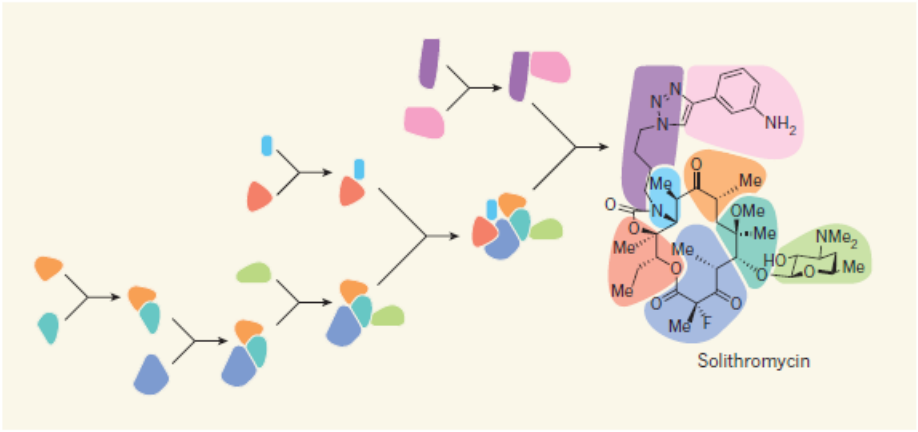

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抗生物質：新規マクロライド系抗生物質探索のための構築基盤

Ian B. Seiple, Ziyang Zhang, Pavol Jakubec, Audrey Langlois-Mercier, Peter M. Wright, Daniel T. Hog, Kazuo Yabu, Senkara Rao Allu, Takehiro Fukuzaki, Peter N. Carlsen, Yoshiaki Kitamura, Xiang Zhou, Matthew L. Condakes, Filip T. Szczypiński, William D. Green & Andrew G. Myers

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ARTICLE

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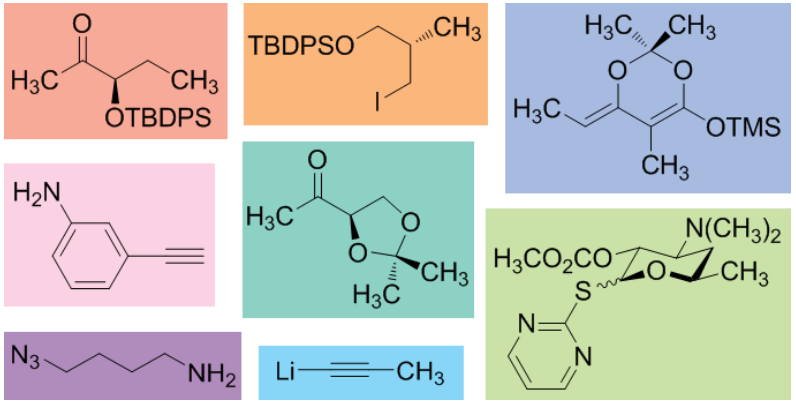
A platform for the discovery of new macrolide antibiotics

Ian B. Seiple[1]*†, Ziyang Zhang[1]*, Pavol Jakubec[1], Audrey Langlois-Mercier[1]†, Peter M. Wright[1]†, Daniel T. Hog[1]†, Kazuo Yabu[1]†, Senkara Rao Allu[1], Takehiro Fukuzaki[1], Peter N. Carlsen[1], Yoshiaki Kitamura[1]†, Xiang Zhou[1], Matthew L. Condakes[1]†, Filip T. Szczypiński[1]†, William D. Green[1]† & Andrew G. Myers[1]

The chemical modification of structurally complex fermentation products, a process known as semisynthesis, has been an important tool in the discovery and manufacture of antibiotics for the treatment of various infectious diseases. However, many of the therapeutics obtained in this way are no longer effective, because bacterial resistance to these compounds has developed. Here we present a practical, fully synthetic route to macrolide antibiotics by the convergent assembly of simple chemical building blocks, enabling the synthesis of diverse structures not accessible by traditional semisynthetic approaches. More than 300 new macrolide antibiotic candidates, as well as the clinical candidate solithromycin, have been synthesized using our convergent approach. Evaluation of these compounds against a panel of pathogenic bacteria revealed that the majority of these structures had antibiotic activity, some efficacious against strains resistant to macrolides in current use. The chemistry we describe here provides a platform for the discovery of new macrolide antibiotics and may also serve as the basis for their manufacture.



Synthesis | Z. Zhang et al. | PSP

An Efficient Directed Claisen Reaction Allows for Rapid Construction of 5,6-Disubstituted 1,3-Dioxin-4-ones

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