A General Approach to the Quinolizidine Alkaloids via an Intramolecular Aza-[3+3] Annulation: Synthesis of (±)-2-Deoxylasubine II

Yu Zhang, Aleksey I. Gerasyuto, Quincy A. Long, Richard P. Hsung*

Division of Pharmaceutical Sciences and Department of Chemistry, University of Wisconsin, 777 Highland Avenue, Rennebohm Hall, Madison, WI 53705, USA
Fax +1(608)2625345; E-mail: rhsung@wisc.edu

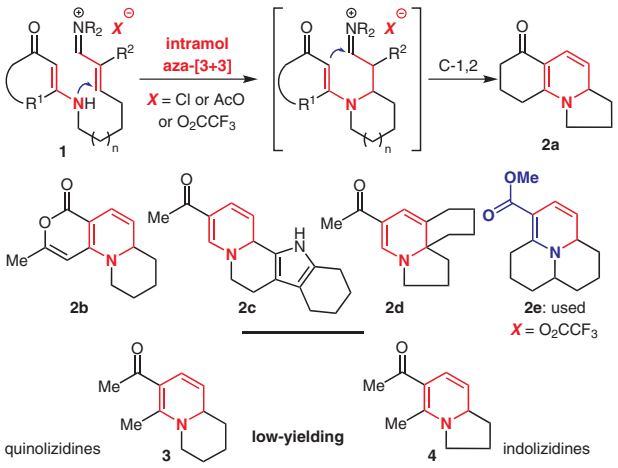
Received 18 September 2008

Abstract: The first success in constructing a member of quinolizidine family of alkaloids employing an intramolecular aza-[3+3] annulation strategy is described here. The key feature is the usage of vinylogous urethane tethered to a vinyl iminium intermediate with trifluoroacetate serving as the counteranion. The proof-of-concept is illustrated with the synthesis of 2-deoxylasubine II.

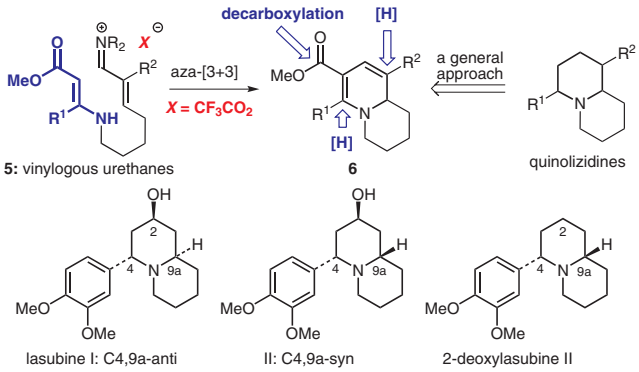
Key words: intramolecular aza-[3+3] annulation, lasubine I, lasubine II, quinolizidines, piperidinium trifluoroacetate salt, Barton's decarboxylation

In the last ten years, we have been developing an aza-[3+3] annulation reaction[1,2] as a general strategy toward alkaloid synthesis.[3,4] The intramolecular variant of this annulation has been particularly useful in natural product synthesis. Specifically, reactions of vinylogous amides **1** (Scheme 1) tethered to a vinyl iminium motif through a tandem sequence of N-1,4-addition and C-1,2-addition[3] can lead to a diverse array of nitrogen heterocycles **2a–e**, which have been applied to a number of total syntheses of alkaloids.[5–8] Despite such success, our annulation strategy has not been useful in approaching simple quinolizidine and indolizidine structural motifs **3** and **4**, which could be accessed only in low yields. Consequently, this limitation precluded us from synthesizing any quinolizidine and indolizidine alkaloids, and limited us to the construction of nitrogen heterocycles **2a–e** with quinolizidine and indolizidine motifs embedded therein.

It was not until recently did we learn that the counteranion [X^-] in these iminium salts plays a significant role in the annulation.[9] In particular, for the synthesis of **2e**,[8b] while iminium salts with acetate as the counteranion were completely ineffective, generating the more reactive trifluoroacetate iminium salt[9] proved to be the solution, rendering a vinylogous urethane deployable for the first time in the aza-[3+3] annulation.[8] We had long recognized a distinct advantage of employing vinylogous urethanes in our aza-[3+3] annulation being that the resulting methoxy carbonyl group in **2e** represents an excellent functional handle for further transformations or removal.[8] Therefore, we investigated annulation reactions of vinylogous urethanes **5** tethered to a trifluoroacetate iminium salt with the intent to develop a general approach toward the quinolizidine



Scheme 1 A deficiency in the aza-[3+3] annulation

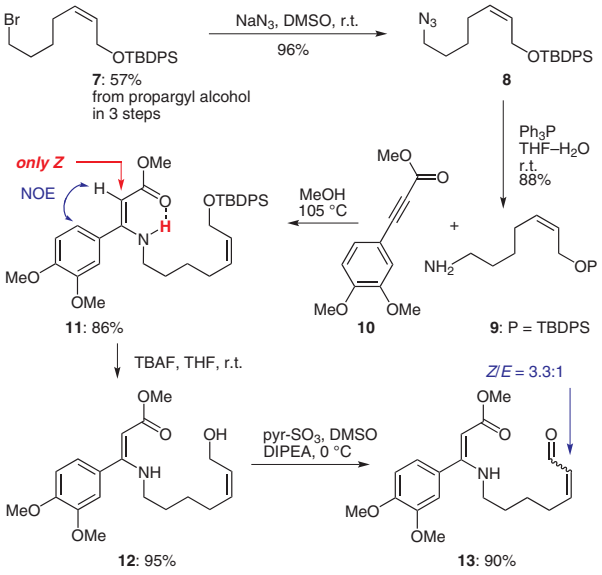


Scheme 2 Establishing a general approach to quinolizidines

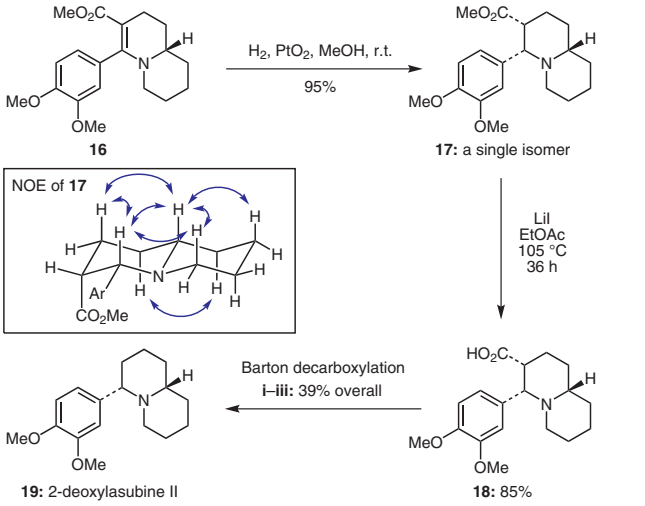
family of alkaloids (Scheme 2). We report here our preliminary success in the synthesis of (±)-2-deoxylasubine II.[10–15]

Our efforts commenced with alkyl bromide **7** prepared from propargyl alcohol in three steps [TBDPS silylation, alkylation with 1,4-dibromobutane, and Lindlar hydrogenation] with an overall yield of 57% (Scheme 3). Displacement of the bromide in **7** with NaN_3 gave azide **8**, and azide reduction using Staudinger's protocol followed by vinylogous urethane formation using alkynoate **10**[16] led to vinylogous urethane **11**[17] in 76% overall yield. Stereochemistry of vinylogous urethane **11** is exclusively *Z* [see NOE] likely due to the favorable internal hydrogen bonding [proton shift of the hydrogen bonded NH: δ =

SYNLETT 2009, No. 2, pp 0237–0240
Advanced online publication: 15.01.2009
DOI: 10.1055/s-0028-1087661; Art ID: S08708ST

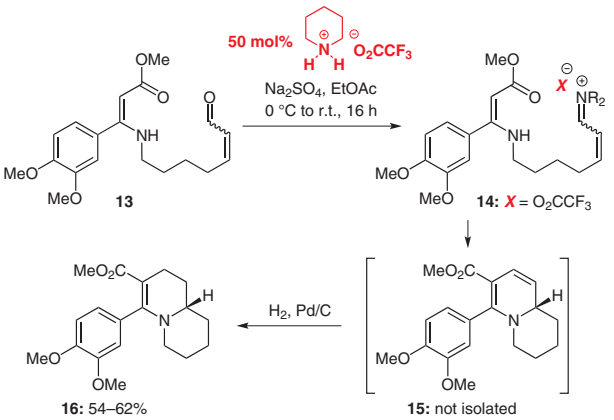


Scheme 3 Synthesis of the vinylogous urethane precursor **13**



Scheme 5 Synthesis of (±)-2-deoxylasubine II. *Reagents and conditions*: (i) $(COCl)_2$, cat. DMF, 0–25 °C; (ii) 2-mercaptopyridine-1-oxide sodium salt, DMAP, 0–25 °C; (iii) *t*-BuSH, *hν*, tungsten lamp, 2 h.

8.48 ppm (t, 1 H, $J = 5.9$ Hz);].[4a,7,8] Desilylation and Parikh–Doering oxidation[18] gave annulation precursor **13** with a *Z*/*E* ratio of 3.3:1 for the enal.



Scheme 4 Sequential aza-[3+3] annulation–hydrogenation

With the vinylogous urethane **13** tethered to the enal in hand, 50 mol% of piperidinium trifluoroacetate salt was used to promote the formation of vinyl iminium intermediate **14**, and an in situ hydrogenation allowed successful isolation of the annulation product **16** in good yield over two operations. Although the initial annulation product **15** could be isolated, it is not as stable as **16** (Scheme 4). It is noteworthy that this work represents the first time our aza-[3+3] annulation method and has succeeded in constructing a simple quinolizidine structural motif such as **16** in a synthetically reliable manner.

Having established the feasibility of this intramolecular aza-[3+3] annulation, we were able to complete a facile synthesis of 2-deoxylasubine II (**19**) employing **16**. As shown in Scheme 5, hydrogenation of the vinylogous urethane in **16** using Adam's catalyst gave ester **17** as a single diastereomer. The assignment of relative stereochemistry in **17** was accomplished using NOE experiments. Lithium iodide promoted demethylation of **17** followed by Barton's standard protocol for decarboxylation gave **19** in 39% overall yield for the sequence.

We have described here our first success in constructing a member of quinolizidine family of alkaloids employing the intramolecular aza-[3+3] annulation strategy. The key feature is the usage of vinylogous urethane tethered to a vinyl iminium ion with trifluoroacetate serving as the counteranion, and the proof-of-concept is shown with the synthesis of 2-deoxylasubine II. Efforts in achieving syntheses of other quinolizidine family members are ongoing.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Acknowledgment

Authors thank NIH [NS38049] for financial support.

References and Notes

(1) For reviews, see: (a) Harrity, J. P. A.; Provoost, O. *Org. Biomol. Chem.* **2005**, *3*, 1349. (b) Hsung, R. P.; Kurdyumov, A. V.; Sydorenko, N. *Eur. J. Org. Chem.* **2005**, 23. (c) Coverdale, H. A.; Hsung, R. P. *Chemtracts* **2003**, *16*, 238.

(2) For recent studies in aza-annulations, see: (a) Hayashi, Y.; Gotoh, H.; Masui, R.; Ishikawa, H. *Angew. Chem. Int. Ed.* **2008**, *47*, 4012. (b) Trost, B. M.; Dong, G. *Org. Lett.* **2007**, *9*, 2357. (c) Schmidt, A.; Gütlein, J.-P.; Mkrrchyan, S.; Görls, H.; Langer, P. *Synlett* **2007**, 1305. (d) Pattenden, L. C.; Wybrow, R. A. J.; Smith, S. A.; Harrity, J. P. A. *Org. Lett.* **2006**, *8*, 3089. (e) Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 6330. (f) Halliday, J. I.; Chebib, M.; Turner, P.; McLeod, M. D. *Org. Lett.* **2006**, *8*, 3399. (g) Katsuyama, I.; Funabiki, K.; Matsui, M.; Muramatsu, H.; Shibata, K. *Heterocycles* **2006**, *68*, 2087. (h) Bose, D. S.;

Kumar, R. K. *Heterocycles* **2006**, *68*, 549. (i) Goodenough, K. M.; Raubo, P.; Harrity, J. P. A. *Org. Lett.* **2005**, *7*, 2993. (j) Goodenough, K. M.; Moran, W. J.; Raubo, P.; Harrity, J. P. A. *J. Org. Chem.* **2005**, *70*, 207. (k) Agami, C.; Dechoux, L.; Hebbe, S.; Ménard, C. *Tetrahedron* **2004**, *60*, 5433. (l) Ji, S.-J.; Jiang, Z.-Q.; Lu, J.; Loh, T.-P. *Synlett* **2004**, 831. (m) Hedley, S. J.; Moran, W. J.; Price, D. A.; Harrity, J. P. A. *J. Org. Chem.* **2003**, *68*, 4286.

(3) For a leading reference on developing our aza-annulations, see: Sklenicka, H. M.; Hsung, R. P.; McLaughlin, M. J.; Wei, L.-L.; Gerasyuto, A. I.; Brennessel, W. W. *J. Am. Chem. Soc.* **2002**, *124*, 10435.

(4) Also see: (a) Ghosh, S. K.; Buchanan, G. S.; Long, Q. A.; Wei, Y.; Al-Rashid, Z. F.; Sklenicka, H. M.; Hsung, R. P. *Tetrahedron* **2008**, *63*, 883. (b) Sydorenko, N.; Hsung, R. P.; Vera, E. L. *Org. Lett.* **2006**, *8*, 2611. (c) Sydorenko, N.; Hsung, R. P.; Darwish, O. S.; Hahn, J. M.; Liu, J. *J. Org. Chem.* **2004**, *69*, 6732. (d) McLaughlin, M. J.; Hsung, R. P.; Cole, K. C.; Hahn, J. M.; Wang, J. *Org. Lett.* **2002**, *4*, 2017. (e) Sklenicka, H. M.; Hsung, R. P.; Wei, L.-L.; McLaughlin, M. J.; Gerasyuto, A. I.; Degen, S. J.; Mulder, J. A. *Org. Lett.* **2000**, *2*, 1161. (f) Hsung, R. P.; Wei, L.-L.; Sklenicka, H. M.; Douglas, C. J.; McLaughlin, M. J.; Mulder, J. A.; Yao, L. J. *Org. Lett.* **1999**, *1*, 509.

(5) For structural types **2a** and **2b**, see: Wei, L.-L.; Sklenicka, H. M.; Gerasyuto, A. I.; Hsung, R. P. *Angew. Chem. Int. Ed.* **2001**, *40*, 1516.

(6) For structural type **2c**, see: (a) Luo, S.; Zificsak, C. Z.; Hsung, R. P. *Org. Lett.* **2003**, *5*, 4709. (b) Sydorenko, N.; Zificsak, C. A.; Gerasyuto, A. I.; Hsung, R. P. *Org. Biomol. Chem.* **2005**, *3*, 2140.

(7) For structural type **2d**, see: (a) Swidorski, J. J.; Wang, J.; Hsung, R. P. *Org. Lett.* **2006**, *8*, 777. (b) Wang, J.; Swidorski, J. J.; Sydorenko, N.; Hsung, R. P.; Coverdale, H. A.; Kuyava, J. M.; Liu, J. *Heterocycles* **2006**, *70*, 423.

(8) For structural type **2e**, see: (a) Gerasyuto, A. I.; Hsung, R. P. *Org. Lett.* **2006**, *8*, 4899. (b) Gerasyuto, A. I.; Hsung, R. P. *J. Org. Chem.* **2007**, *72*, 2476.

(9) For an asymmetric intramolecular aza-[3+3] annulation, see: Gerasyuto, A. I.; Hsung, R. P.; Sydorenko, N.; Slafer, B. W. *J. Org. Chem.* **2005**, *70*, 4248.

(10) For isolations of (±)-lasubine I and II, see: (a) Fuji, K.; Yamada, K.; Fujita, E.; Murata, H. *Chem. Pharm. Bull.* **1978**, *26*, 2515. (b) For a leading review in quinolizidine alkaloids, see: Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 139; and references cited therein.

(11) For syntheses of (±)-lasubine I and II, see: (a) Iida, H.; Tanaka, M.; Kibayashi, C. *J. Chem. Soc., Chem. Commun.* **1983**, *20*, 1143. (b) Iida, H.; Tanaka, M.; Kibayashi, C. *J. Org. Chem.* **1984**, *49*, 1909. (c) Ent, H.; De Koning, H.; Speckamp, W. N. *Heterocycles* **1988**, *27*, 237. (d) Bardot, V.; Gardette, D.; Gelas-Mialhe, Y.; Gramain, J.-C.; Remuson, R. *Heterocycles* **1998**, *48*, 507. (e) Narasaka, K.; Yamazaki, S.; Ukaji, Y. *Chem. Lett.* **1985**, 1177. (f) Hoffmann, R. W.; Endesfelder, A. *Liebigs Ann. Chem.* **1986**, 1823. (g) Brown, J. D.; Foley, M. A.; Comins, D. L. *J. Am. Chem. Soc.* **1988**, *110*, 7445. (h) Pilli, R. A.; Dias, L. C.; Maldaner, A. O. *Tetrahedron Lett.* **1993**, *34*, 2729. (i) Pilli, R. A.; Dias, L. C.; Maldaner, A. O. *J. Org. Chem.* **1995**, *60*, 717. (j) Ukaji, Y.; Ima, M.; Yamada, T.; Inomata, K. *Heterocycles* **2000**, *52*, 563.

(12) For syntheses of (–)-lasubine I, see: (a) Chalard, P.; Remuson, R.; Gelas-Mialhe, Y.; Gramain, J.-C. *Tetrahedron: Asymmetry* **1998**, *9*, 4361. (b) Kundig, P. E.; Ratni, H. *Org. Lett.* **1999**, *1*, 1997. (c) Davis, F. A.; Roa, A.; Carroll, P. J. *Org. Lett.* **2003**, *5*, 3855. (d) Kundig, P. E.; Cannas, R.; Fabritius, C.-H.; Grossheimann, G.; Kondratenko, M.; Laxmisha, M.; Pache, S.; Ratni, H.; Robvieux, F.; Romanens, P.; Tchertchian, S. *Pure Appl. Chem.* **2004**, *76*, 689. (e) Liu, S.; Fan, Y.; Peng, X.; Wang, W.; Hua, W.; Akber, H.; Liao, L. *Tetrahedron Lett.* **2006**, *47*, 7681.

(13) For syntheses of (+)-lasubine I, see: Mancheno, O. G.; Arrayas, R. G.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2007**, *72*, 10294.

(14) For syntheses of (–)-lasubine II, see: (a) Comins, D. L.; LaMunyon, D. H. *J. Org. Chem.* **1992**, *57*, 5809. (b) Chalard, P.; Remuson, R.; Gelas-Mialhe, Y.; Gramain, J.-C. *Tetrahedron: Asymmetry* **1998**, *9*, 4361. (c) Davis, F. A.; Chao, B. *Org. Lett.* **2000**, *2*, 2623. (d) Ma, D.; Zhu, W. *Org. Lett.* **2001**, *3*, 3927. (e) Hamilton, M. D.; Back, T. G. *Org. Lett.* **2002**, *4*, 1779. (f) Gracias, V.; Zeng, Y.; Desai, P.; Aubé, J. *Org. Lett.* **2003**, *5*, 4999. (g) Blechert, S.; Zaja, M. *Tetrahedron* **2004**, *60*, 9629. (h) Back, T. G.; Hamilton, M. D.; Lim, V. J. J.; Parvez, M. *J. Org. Chem.* **2005**, *70*, 967. (i) Liu, S.; Hua, W.; Haji, A.; Liao, L.; Wang, W. *Zhongguo Yaoke Daxue Xuebao* **2007**, *38*, 193. (j) Kim, G.; Lim, J. *Tetrahedron Lett.* **2008**, *49*, 88.

(15) For syntheses of (+)-lasubine II, see: (a) Yu, R. T.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*, 12370. (b) Mancheno, O. G.; Arrayas, R. G.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2007**, *72*, 10294.

(16) For a synthesis of **10**, see: O'Malley, S. J.; Tan, K. L.; Watzke, A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 13496.

(17) **Selected Experimental Procedures and Characterizations**

Aza-[3+3] Annulation

To a stirring heterogeneous suspension of enal **13** (2.81 g, 8.09 mmol) and grounded Na_2SO_4 (flame-dried, 9.00 g) in freshly distilled anhyd EtOAc (180 mL) was added piperidinium trifluoroacetate salt (796.0 mg, 4.00 mmol) at 0 °C. The resulting suspension was allowed to warm up to r.t. slowly. After 16 h, NMR showed complete consumption of the aldehyde. To this reaction mixture was added Pd/C (869.0 mg, 0.81 mmol), and the flask was filled with H_2 gas by five evacuate–back-fill cycles. After which, the mixture was stirred under H_2 at r.t. for 6 h. The mixture was then filtered through Celite™ to remove the solid, and the solution was concentrated in vacuo to give a reddish oil. The crude product was purified by silica gel flash column chromatography buffered with Et_3N (isocratic eluent: EtOAc–hexanes, 1:2) to give the desired annulation product **16** (1.65 g, 4.98 mmol) in 62% yield as yellow solid. Compound **16**: R_f = 0.32 (EtOAc–hexanes, 1:2); mp 114–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21–1.25 (m, 1 H), 1.36–1.42 (m, 3 H), 1.66–1.75 (m, 2 H), 1.78 (d, 1 H, *J* = 6.4 Hz), 1.95 (dd, 1 H, *J* = 6.5, 13.1 Hz), 2.37–2.54 (m, 3 H), 3.11–3.14 (m, 2 H), 3.36 (s, 3 H), 3.83 (s, 3 H), 3.86 (s, 3 H), 6.63 (s, 1 H), 6.67 (d, 1 H, *J* = 8.2 Hz), 6.82 (d, 1 H, *J* = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 24.5, 26.5, 29.0, 32.7, 49.5, 50.3, 55.6, 55.8, 57.0, 95.9, 109.7, 110.6, 120.8, 130.9, 148.2, 148.6, 156.1, 168.9. IR (neat): 2940 (s), 1643 (s), 1562 (s), 1511 (s), 1122 (s) cm^{-1}. MS (APCI): *m/e* (relative intensity) = 332 (100) $[M + H]^+$; *m/e* calcd for $C_{19}H_{25}NO_4Na$: 354.1676; found: 354.1679.

Hydrogenation

To a flame-dried 100 mL round-bottom flask was added PtO_2 (102.0 mg, 0.45 mmol) and MeOH (10 mL). The flask was filled with H_2 by three evacuate–back-fill cycles and the resulting suspension was stirred at r.t. for 20 min, and the original brown powder of PtO_2 turned into black sponge. To this heterogeneous mixture was added via syringe a solution of the freshly purified annulation product **16** (296.0 mg, 0.89

mmol) in MeOH (30 mL). The resulting mixture was stirred at r.t. for 16 h and TLC showed complete conversion of the starting material. The solution was filtered through Celite™ and concentrated in vacuo. The crude product was purified by silica gel flash column chromatography buffered with Et_3N (isocratic eluent: EtOAc–hexanes, 1:4) to give ester **17** (258.0 mg, 0.77 mmol) in 87% yield as colorless oil.

Compound **17**: R_f = 0.26 (EtOAc–hexanes, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (tq, 1 H, *J* = 4.3, 12.5 Hz), 1.35–1.44 (m, 3 H), 1.46–1.58 (m, 3 H), 1.61–1.70 (m, 2 H), 1.87 (1 H, tt, *J* = 4.5, 13.0 Hz), 1.87–1.91 (m, 1 H), 2.11 (1 H, dq, *J* = 3.6, 13.0 Hz), 2.70 (t, 1 H, *J* = 4.5 Hz), 2.78–2.81 (m, 1 H), 3.09 (d, 1 H, *J* = 4.4 Hz), 3.30 (s, 3 H), 3.80 (s, 3 H), 3.81 (s, 3 H), 6.71–6.76 (m, 2 H), 6.86 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.9, 26.0, 26.7, 28.7, 33.6, 47.3, 50.7, 53.9, 55.7, 55.8, 63.3, 69.9, 110.3, 110.5, 119.7, 134.9, 147.7, 148.6, 173.6. IR (neat): 2929 (s), 1735 (s), 1591 (s), 1259 (s), 1152 (s) cm^{-1}. MS (APCI): *m/e* (relative intensity) = 334 (100) $[M + H]^+$; *m/e* calcd for $C_{19}H_{27}NO_4Na$: 356.1832; found: 356.1848.

Demethylation of Ester 17

To a solution of ester **17** (112 mg, 0.336 mmol) in freshly distilled EtOAc (7 mL) was added LiI (270 mg, 2.02 mmol). The resulting solution was deoxygenated via purging with Argon gas for 15 min, and then the reaction vessel was sealed under Argon, wrapped with aluminum foil, and heated in a 105 °C oil bath. After heating for 36 h, the solution was cooled down to r.t. and filtered. The light brown solid filter cake was washed with EtOAc (3 mL) and Et_2O (2 mL), and dried in vacuo to give a brown solid. The solid salt was then dissolved in H_2O (10 mL), and acidified via dropwise addition of 1.0 N aq HCl solution until the pH value of the aqueous solution reached 3–4. The aqueous solution was then saturated with solid NaCl, and extracted with $CHCl_3$ (6 × 8 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to give product acid **18** (91.0 mg, 0.29 mmol) in 85% yield as a light brown solid. Acid **18** was used immediately for decarboxylation.

Barton's Decarboxylation

To a solution of acid **18** (130.0 mg, 0.41 mmol) in anhyd CH_2Cl_2 (10 mL) was added one drop of DMF. The solution was stirred at 0 °C for 2 min before oxalyl chloride (104.0 mg, 0.82 mmol) was added via syringe. The resulting solution was allowed to warm up to r.t. over 30 min, and was stirred at r.t. for an additional 1 h. After which, a high vacuum (0.665–1.33 mbar) was slowly applied to remove solvent and volatile materials. The residual material was then further dried under high vacuum for 30 min, before it was dissolved in anhyd CH_2Cl_2 (8 mL) and transferred via syringe to a chilled solution of 2-mercaptopyridine-1-oxide sodium salt (122.0 mg, 0.82 mmol) and DMAP (10 mg, 0.08 mmol) in anhyd CH_2Cl_2 (8 mL). The resulting suspension was stirred at 0 °C with the flask shielded from light using Al foil. It was then slowly warmed up to r.t. and stirred at r.t. for 1.5 h.

After which, *t*-BuSH (587.0 mg, 6.50 mmol) was added via syringe all at once and the yellowish suspension was then irradiated with a 300 W tungsten lamp for 3 h with the solution cooled by a water bath. Solvent and excess of *t*-BuSH was then removed in vacuo, and 5% aq $NaHCO_3$ (30 mL) solution was added. The aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with sat. aq NaCl (10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by silica gel flash column chromatography buffered with Et_3N (isocratic eluent: EtOAc–hexanes, 1:4) to give product (±)-2-deoxylasubine II (**19**, 44.0 mg, 0.16 mmol) in 39% yield as colorless oil, which solidified upon standing.

Compound **19**: R_f = 0.29 (EtOAc–hexanes, 1:4); mp 68–70 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (tt, 1 H, *J* = 4.3, 11.5 Hz), 1.33–1.47 (m, 5 H), 1.54–1.61 (m, 4 H), 1.63–1.75 (m, 3 H), 1.87–1.92 (t, 1 H, *J* = 10.5 Hz), 2.66 (d, 1 H, *J* = 9.3 Hz), 2.82 (dd, 1 H, *J* = 2.9, 10.9 Hz), 3.85 (s, 3 H), 3.88 (s, 3 H), 6.76–6.89 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.8, 24.9, 26.2, 33.7, 33.8, 36.5, 53.5, 55.7, 55.9, 63.4, 70.2, 110.3, 110.7, 119.5, 138.2, 147.6, 148.9. IR (neat): 2926 (s), 1502 (s), 1147 (s) cm^{-1}. MS (APCI): *m/e* (relative intensity) = 276 (100) $[M + H]^+$; *m/e* calcd for $C_{17}H_{26}NO_2$: 276.1958; found: 276.1958.

(18) See: Parikh, J. R.; von Doering, W. E. *J. Am. Chem. Soc.* **1967**, *89*, 5505; this is the only oxidation in which the *Z*-geometry of the vinylogous urethane does not scramble.