

A Pyridine Dearomatization Approach to the Matrine-Type Lupin Alkaloids

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ABSTRACT: (+)-Matrine and (+)-isomatrine are tetracyclic alkaloids isolated from the plant *Sophora flavescens*, the roots of which are used in traditional Chinese medicine. Biosynthetically, these alkaloids are proposed to derive from three molecules of (–)-lysine via the intermediacy of the unstable cyclic imine Δ^1 -piperidine. Inspired by the biosynthesis, a new dearomative annulation reaction has been developed that leverages pyridine as a stable surrogate for Δ^1 -piperidine. In this key transformation, two molecules of pyridine are joined with a molecule of glutaryl chloride to give the complete tetracyclic framework of the matrine alkaloids in a single step. Using this dearomative annulation, isomatrine is synthesized in four steps from inexpensive commercially available chemicals. Isomatrine then serves as the precursor to additional lupin alkaloids, including matrine, allomatrine, isosophoridine, and sophoridine.

The lupin alkaloids are a structurally diverse class of quinolizidine-containing natural products isolated from plants in the *Lupinus* genus (Figure 1A).¹ (+)-Matrine (2), the primary component of Chinese Kushen injection, inhibits proliferation in metastatic cancer cell lines and has also been investigated as a therapeutic agent against encephalomyelitis, asthma, arthritis, and osteoporosis.^{2,3} (–)-Sophoridine (4) is an approved chemotherapeutic in China, which has also demonstrated antibiotic activity.⁴ Little is known about the pharmacological properties of (+)-isomatrine (1) and (+)-isosophoridine (5), which likely reflects their limited accessibility from commercial vendors.⁵

Although the detailed enzymatic pathway has not been fully annotated, the biosynthesis of matrine is proposed to initiate with the enzymatic conversion of (–)-lysine (6) to Δ^1 -piperidine (7) (Figure 1B).^{6,7} Subsequent dimerization of 7 followed by oxidation and isomerization is proposed to yield quinolizidine 8, a shared biosynthetic precursor to several lupin alkaloids.^{8,9} Mannich addition of 8 to a third equivalent of 7 and cyclization with the pendant aldehyde is proposed to generate the oxidized tetracycle 9, which upon reduction gives (+)-matridine (10). Seminal studies by Abdusalamov demonstrated that feeding ¹⁴C-labeled (+)-10 to *Goebelia Pachycarpa* resulted in the isolation of radio-labeled (+)-2, suggesting that the final step in the biosynthesis of 2 is a site-selective C–H oxidation.^{10,11}

Synthetically, most of the work prior to 2022 had focused on matrine (2), with four reported total syntheses.^{12–15} Synthetic access to the minor congeners is far more limited: until a recent report by Sherburn and co-workers,¹⁶ there was a single total synthesis each of allomatrine (3) and isosophoridine (5), and no reported total syntheses of isomatrine or sophoridine (4).^{17,18} We sought to devise a unified synthesis that could provide access to the series of matrine-type alkaloids shown in Figure 1A. Inspired by the proposed biosynthesis, it was envisioned that pyridine (14) could serve as a stable, inexpensive synthon for Δ^1 -piperidine (7), and the remaining five carbons of the

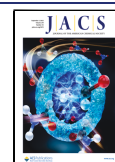
tetracyclic matrine framework could derive from glutaryl chloride (15, Figure 1C). In the key step, we proposed a dearomative annulation via bis-acylpyridinium salt 17 to form tetracycle 12, a molecule that contains all the C and N atoms of 1.¹⁹ Tetracycle 12 could be elaborated to 1 by global reduction followed by a site-selective oxidation of isomatridine (11) reminiscent of the proposed biosynthesis of matrine (2). Isomatrine (1) is the least thermodynamically stable of alkaloids 1–5 and its isomerization to both 2 and 3 has been previously reported.²⁰ Therefore, we anticipated that access to 1 could enable the synthesis of additional lupin alkaloids.²¹ This type of late-stage isomerization strategy was also deployed in the 2022 Sherburn synthesis of several matrine alkaloids.¹⁶

Our studies commenced with the investigation of the dearomative annulation (Figure 2A). Addition of glutaryl chloride (15) to pyridine (14) in dichloromethane at –50 °C, followed by warming to 21 °C, resulted in the clean formation of (±)-tetracycle 12 in 62% yield (10 g scale). The reaction was highly robust and could be performed on one mole scale to produce over 160 g (67% yield) of (±)-tetracycle 12 in a single batch. The product was isolated by precipitation from the crude reaction mixture, alleviating the need for a workup or column chromatography. Given the cost of pyridine (\$7/mol), glutaryl chloride (\$211/mol), and all solvents (\$31/mol), the raw materials cost \$398/mol of product formed.²² Recrystallization of (±)-12 enabled single-crystal X-ray diffraction, which confirmed the *syn-syn* relative stereochemistry.²³

To elucidate the reaction pathway, mechanistic and computational studies were undertaken. Monitoring the reaction

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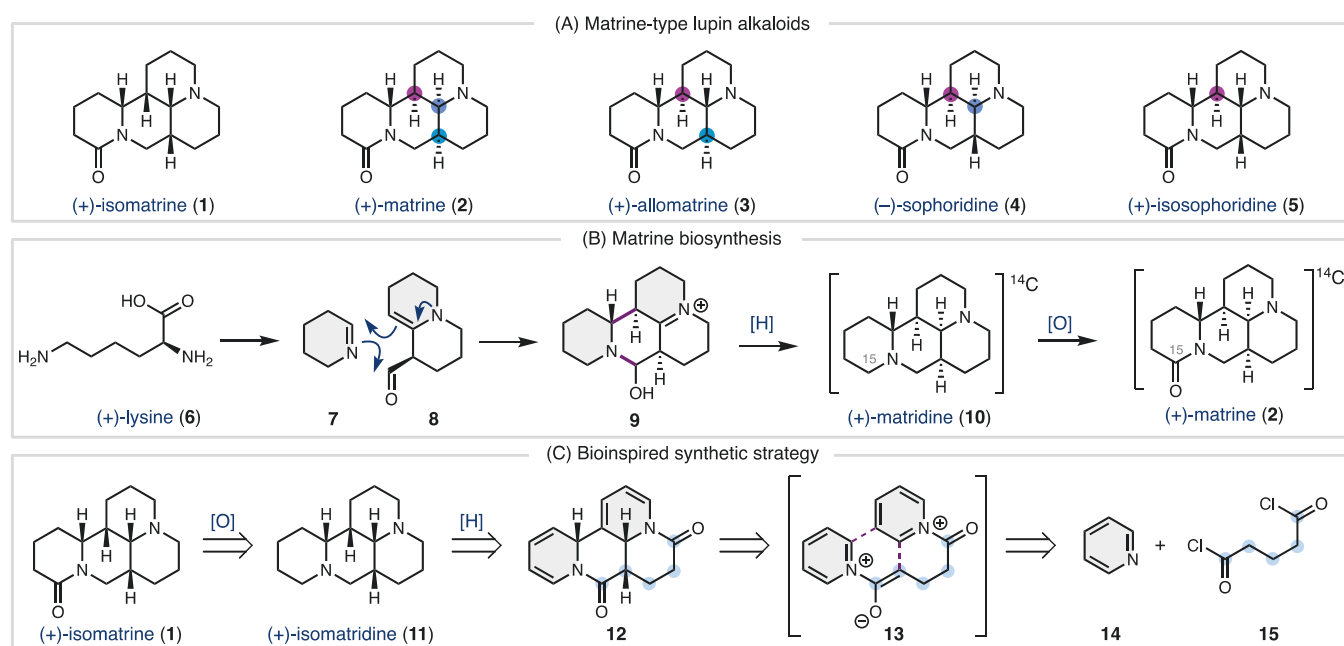


Figure 1. (A) Chemical structures of matrine-type lupin alkaloids. (B) Proposed biosynthesis of matrine. (C) Retrosynthetic analysis of isomatrine.

between **14** and **15** by ^1H NMR determined that the major species at -40°C was bis-acylpyridinium salt **17** (Figure 2C). After warming to 25°C , acid chloride **18** resulting from monocyclization was observed. Presumably the acylpyridinium salt **Int1a** and acyl chloride **18** are in equilibrium, but the acyl chloride is the major species at 25°C . A second, minor species assigned as the acid chloride resulting from **Int1b** (vide infra) was also observed; this species was consumed as the reaction progressed to full conversion.²³ Although deprotonation of acylpyridinium salts or acyl chlorides can give rise to ketene intermediates,²⁴ no such species was detected by ^1H NMR or by reactIR. Attempts to calculate a pathway involving ketene intermediates failed to locate a transition state (TS) for a concerted $[2 + 2]$ cycloaddition. Similarly, no TS for the concerted $[4 + 2]$ cycloaddition of bis-acylpyridinium salt **13** could be located. Investigation of a stepwise pathway determined that the lowest-energy TS for the first cyclization involves a boatlike conformation to form the *syn* product (TS1a, $\Delta G_{\text{TS}} = 7.3$ kcal/mol) (Figure 2D). Attempts to find the analogous chairlike TS were unsuccessful and, instead, led to conversion to the boatlike TS. The pathways leading to the *anti* monocyclization product (**Int1b**) are higher in energy (see TS1b and TS1c). The preference for the *syn* boat, compared to the *anti* boat TS, is likely due to favorable dispersive interactions between the heteroaryl ring and the oxygen-bearing carbon of the enolate, as well as minimization of the dipole moment in the *syn* TS. In order to test the importance of dispersive interactions in these TSs, the TSs were recomputed with B3LYP, a functional known to lack dispersion. Indeed, with this functional, the difference between the two transition states was only 0.1 kcal/mol. Inclusion of dispersion with Grimme's D3 correction restored the energy difference to 1.4 kcal/mol in favor of the *syn* boat transition state.

These TSs lead to two intermediates: *syn* intermediate **Int1a** (-12.6 kcal/mol) and *anti* intermediate **Int1b** (-10.7 kcal/mol). The TS for the second C–C bond formation (TS2a) is most favorable for the *syn-syn* intermediate (**Int2a**), with a barrier of 20.2 kcal/mol. The second lowest-energy pathway

proceeds via TS2b, leading to **Int2b**, which gives rise to the *anti-syn-anti* configuration at the ring fusions. The transition states leading to the other four potential diastereomers are higher in energy. Formation of **Int2a** and **Int2b** is followed by deprotonation by pyridine. While **Int2b** is lower in energy than **Int2a**, the deprotonation of **Int2a** to give *syn-syn* ($\pm$)-**12** follows the lowest-energy pathway. Thus, the selectivity-determining step is the final deprotonation (TS3a) and *syn-syn* ($\pm$)-**12** is favored, even though it is thermodynamically less stable than *anti-anti*-**19**. These results are consistent with the experimentally observed formation of product ($\pm$)-**12** as a single diastereomer, despite the initial mixture of monocyclization products. When enantiopure (*R*)-2-methylpentandioyl chloride was employed, C3-methyl tetracycle (+)-**16** was obtained in 66% yield as a single diastereomer and in >99% enantiomeric excess (ee) (Figure 2B). This stereochemical outcome is consistent with the calculations, where the pathway initiating with a *syn* boat transition state bearing the methyl group in a pseudoequatorial position is favored.

At this stage, attention turned to elaborating ($\pm$)-**12** to isomatrine (**1**) (Figure 3A). Hydrogenation of tetraene **12** proceeded smoothly, followed by reduction with alane to give ($\pm$)-isomatridine (**11**) in 60% yield over two steps. Purification was readily accomplished by generating the hydrogen oxalate salt, followed by trituration in acetone, obviating the need for column chromatography. At this stage, resolution of diamine ($\pm$)-**11** can be achieved by recrystallization of the di-*p*-toluoyl tartaric acid salt to give 24% recovery (46% theoretical yield) of the desired (+)-diamine **11** in 90% ee.

Inspired by the proposed biosynthesis,²⁵ we initially investigated the enzymatic oxidation of (+)-**11** to give (+)-**1**. Unfortunately, a screen of >180 bacterially derived P450 enzymes (both wild type and mutants) failed to produce any promising leads. As a result, our focus turned toward nonenzymatic methods for the selective oxidation of C15. Analysis of the X-ray structure of diamine **11** revealed that the N1 lone pair points into the cavity of the molecule while the N2 lone pair points outward. Selective oxidation of N2 was achieved

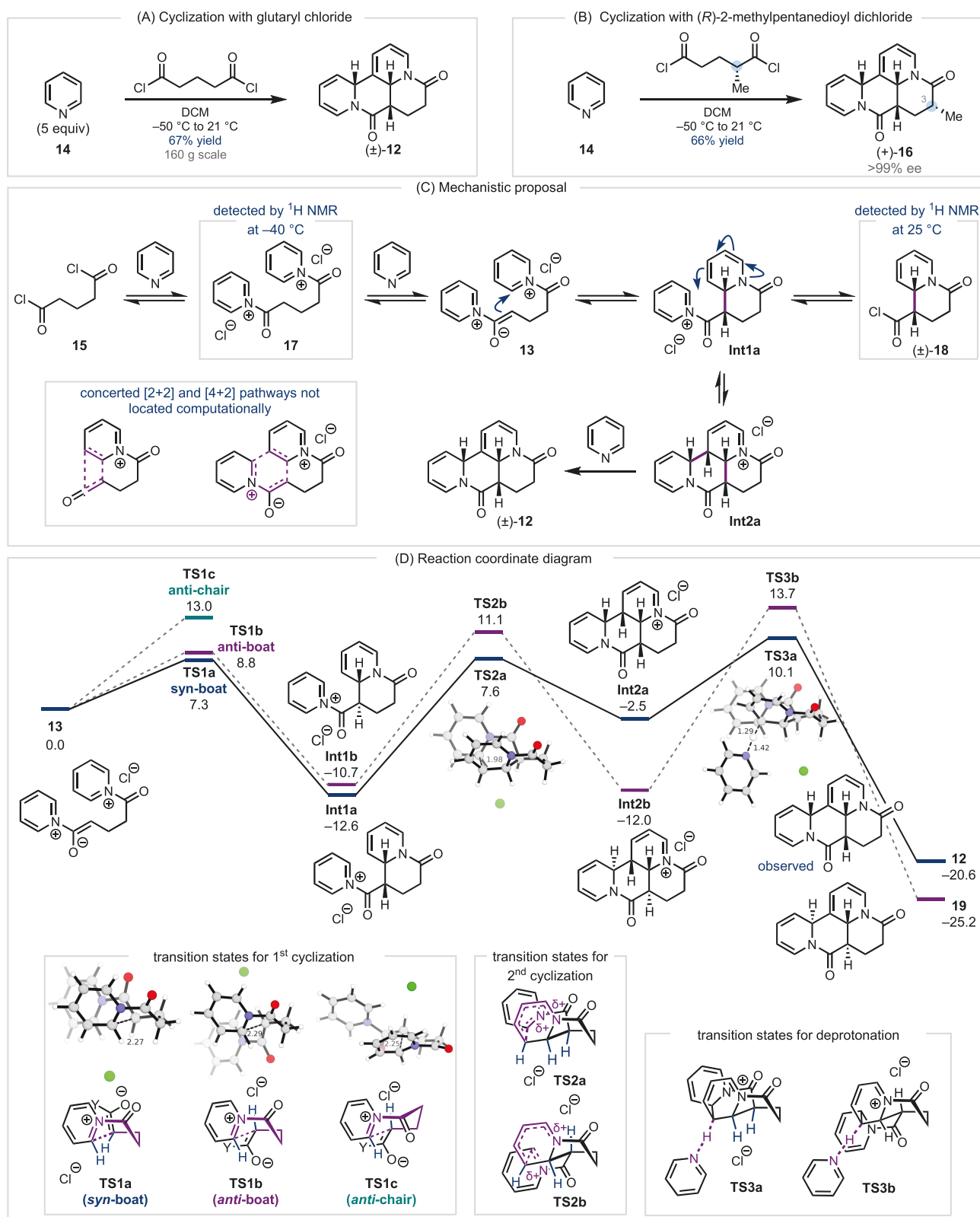


Figure 2. (A) Diastereoselective cyclization of pyridine and glutaryl chloride. (B) Diastereoselective cyclization of (*R*)-2-methylpentanedioyl chloride. (C) Proposed mechanism for the diastereoselective cyclization. (D) Reaction coordinate diagram performed with Gaussian, using ω B97XD/def2-TZVP/SMD(DCM).

by treatment of diamine **11** with peracetic acid to yield the expected *N*-oxide **20** in a 54% yield. However, attempts to advance **20** via Polonovski reaction (acetic anhydride/2,6-di-*tert*-butyl-4-methylpyridine (DTBMP)) led to formation of the

undesired enamine **21**.²⁶ Analysis of the X-ray structure of **20** confirmed that antiperiplanar alignment of H17 with the N–O bond is ideally suited to regioselectively form the undesired elimination product **21**.

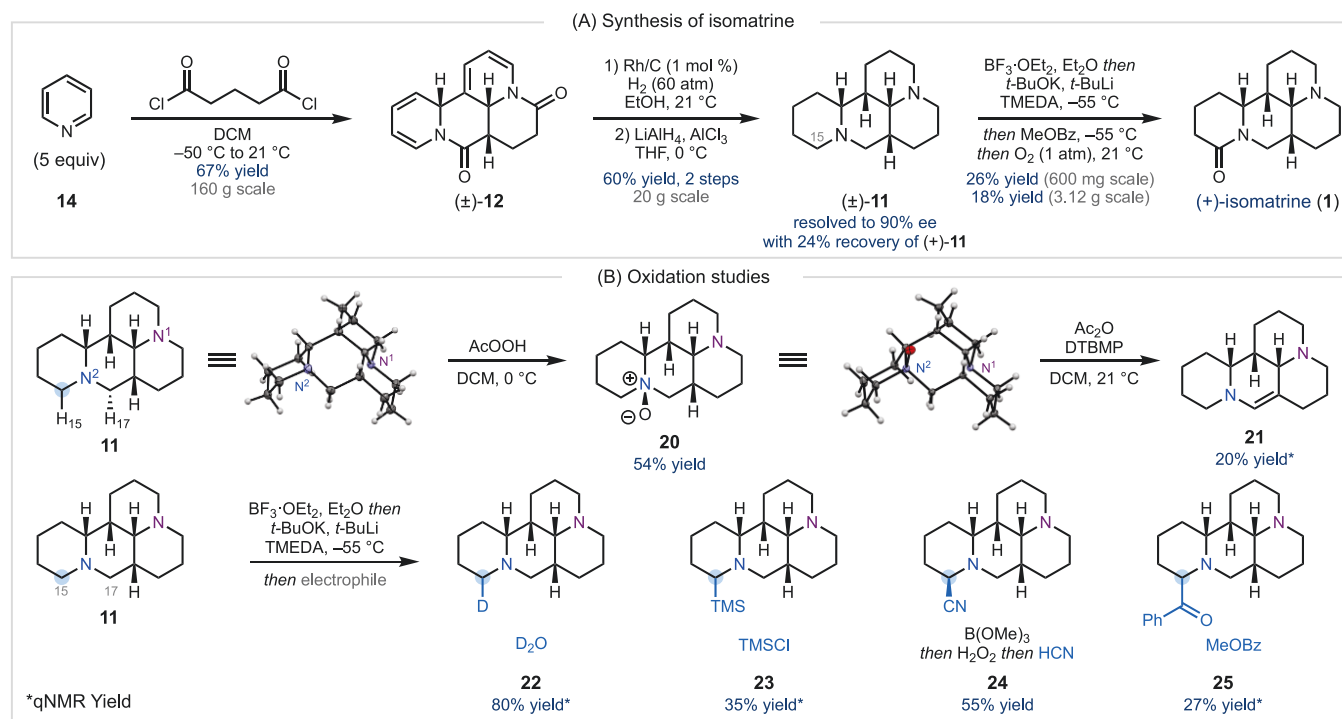


Figure 3. (A) Complete total synthesis of isomatrine. (B) Attempted oxidation reactions.

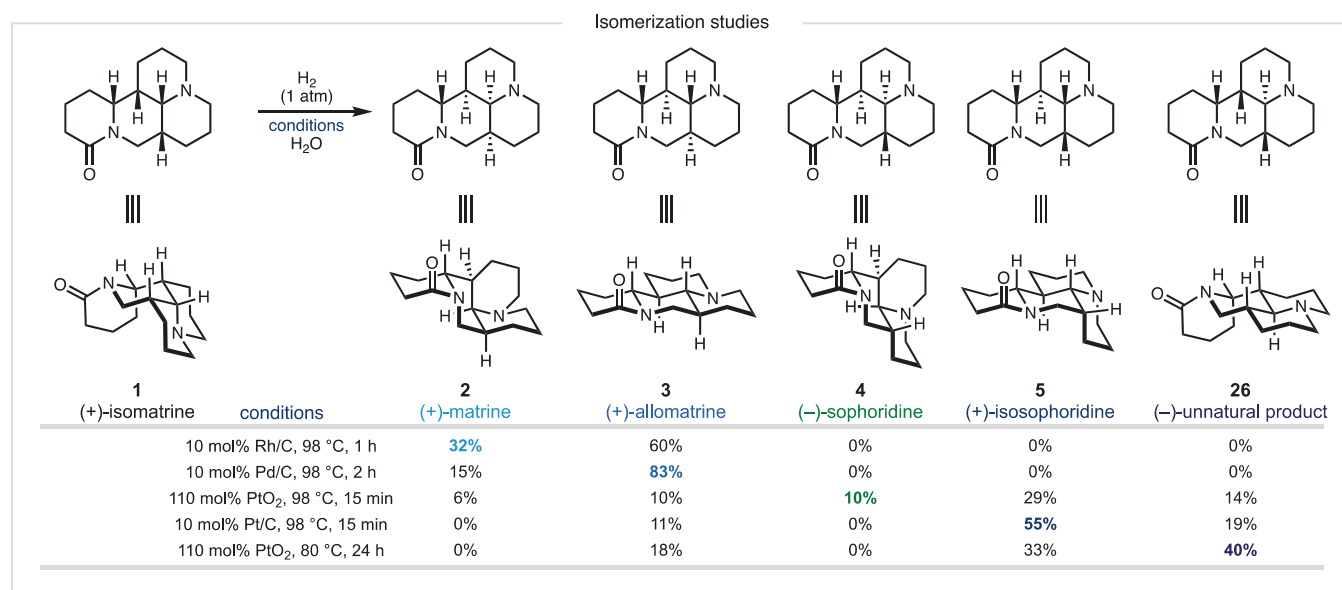


Figure 4. Isomerization of (+)-isomatrine to additional matrine-type lupin alkaloids. Highlighted values are the isolated yields of the indicated products.

We became interested in a report by Kessar and co-workers demonstrating that amine–BF₃ adducts could undergo deprotonation using mixtures of *tert*-butyl lithium (*t*-BuLi) and potassium *tert*-butoxide (*t*-BuOK).²⁷ Consistent with the selectivity in the *N*-oxide formation, treatment of diamine (+)-11 with BF₃·OEt₂ quantitatively formed the Lewis acid–base complex. Deprotonation of the BF₃ complex of (+)-11 with a mixture of *t*-BuLi and *t*-BuOK in *N,N,N,N*-tetramethylethylenediamine (TMEDA) occurred with good selectivity for the less sterically encumbered C15 over C17 (10:1), as determined by trapping with deuterated methanol (22, Figure 3B).²⁸ Unfortunately, trapping of this anion with other electrophiles

proved more challenging. For example, deprotonation followed by quenching with TMSCl provided silylated diamine 23 in only 35% yield, while trapping with methyl benzoate gave unstable phenyl ketone 25 in 27% yield. The best yield of C15-functionalized product was obtained when 11 was deprotonated and then trapped with trimethyl borate; oxidation with hydrogen peroxide and trapping of the resultant enamine with HCN gave aminonitrile 24 in 55% yield. Aerobic oxidation of 24 provided isomatrine in 46% yield (25% yield over three steps from 11).^{23,29} Alternatively, deprotonation of (+)-11, trapping with methyl benzoate, and aerobic oxidation could be performed in a single reaction flask to give (+)-1 directly in yields of 18%–

26%, depending on the scale.³⁰ This route provides access to (±)-isomatrine in four steps, and (+)-isomatrine can be easily accessed by incorporating the resolution of diamine **11**. To date, >1 g of (+)-isomatrine has been prepared.

Initial attempts to reproduce Okuda's Pt-catalyzed isomerization of (+)-isomatrine failed to provide the reported yields of (+)-matrine (**2**) and (+)-allomatrine (**3**), and instead produced a mixture of five compounds.²⁰ To improve the yield of **2** and **3**, while also broadening the synthetic access to other congeners, an investigation of several isomerization catalysts was performed. Use of Rh/C provided the best yields of (+)-**2** (32% yield, Figure 4), while (+)-**3** could be obtained in 83% yield when Pd/C was used. Isomerization with Pt/C provided (+)-isosophoridine (**5**) in 55% yield. Finally, use of PtO₂ at 98 °C for 15 min furnished (−)-sophoridine (**4**) in 10% yield, together with the other isomers.^{31,32} When the reaction with PtO₂ was conducted at 80 °C for 24 h, (−)-isomer **26** was isolated in 40% yield. To our knowledge, **26** has not yet been isolated from natural sources.

The bioinspired dearomative annulation between pyridine and glutaryl chloride developed here has enabled the first total synthesis of the lupin alkaloid (−)-sophoridine, and the shortest syntheses of (+)-isomatrine, (+)-matrine, (+)-allomatrine, and (+)-isosophoridine reported to date. The brevity of this route results from the ability to construct the entire carbon framework of the matrine-type alkaloids in a single step. The diversity of matrine-type alkaloids prepared from commodity chemicals is anticipated to support future pharmacological investigations.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.2c06584>.

Experimental procedures, characterization data (¹H and ¹³C NMR, HRMS, FTIR) for all new compounds, coordination geometries for DFT optimized compounds (PDF)

FIDs for NMR data (ZIP)

Accession Codes

CCDC 2159764–2159768, 2159770–2159774, and 2163777 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) Ohmiya, S.; Saito, K.; Murakoshi, I. Chapter 1 Lupine alkaloids. In *The Alkaloids: Chemistry and Pharmacology*. Cordell, G. A., Ed.; Academic Press, 1995; pp 1–114.
- (2) Zhang, H.; Chen, L.; Sun, X.; Yang, Q.; Wan, L.; Guo, C. Matrine: A promising natural product with various pharmacological activities. *Front. Pharmacol.* **2020**, *11*, 588.
- (3) You, L.; Yang, C.; Du, Y.; Wang, W.; Sun, M.; Liu, J.; Ma, B.; Pang, L.; Zeng, Y.; Zhang, Z.; Dong, X.; Yin, X.; Ni, J. A systematic review of the pharmacology, toxicology and pharmacokinetics of matrine. *Front. Pharmacol.* **2020**, *11*, 01067.
- (4) Wang, Q.; Li, Y.; Li, K.-W.; Zhou, C.-Z. Sophoridine: A review of its pharmacology, pharmacokinetics and toxicity. *Phytomedicine* **2022**, *95*, 153756.
- (5) No vendors were found to stock either (+)-isomatrine or (+)-isosophoridine as found by a CAS SciFinder supplier search (June 14, 2022) and an eMolecule supplier search (June 14, 2022).
- (6) Bunsupa, S.; Katayama, K.; Ikeura, E.; Oikawa, A.; Toyooka, T.; Saito, K.; Yamazaki, M. Lysine decarboxylase catalyzes the first step of quinolizidine alkaloid biosynthesis and coevolved with alkaloid production in leguminosae. *Plant Cell* **2012**, *24*, 1202–1216.
- (7) Yang, T.; Nagy, I.; Mancinotti, D.; Otterbach, S. L.; Andersen, T. B.; Motawia, M. S.; Asp, T.; Geu-Flores, F. Transcript profiling of a

bitter variety of narrow-leafed lupin to discover alkaloid biosynthetic genes. *J. Exp. Bot.* **2017**, *68*, 5527–5537.

(8) Golebiewski, W. M.; Spenser, I. D. Biosynthesis of the lupine alkaloids. II. Sparteine and lupanine. *Can. J. Chem.* **1988**, *66*, 1734–1748.

(9) Mancinotti, D.; Frick, K. M.; Geu-Flores, F. *Nat. Prod. Rep.* **2022**, *39*, 1423–1437.

(10) Abdusalamov, B. A. Biosynthesis and metabolism of some matrine alkaloids in *Goebelia pachycarpa*. *Chem. Nat. Compd.* **1984**, *20*, 1–9.

(11) Leeper, F. J.; Grue-Sørensen, G.; Spenser, I. D. Biosynthesis of the quinolizidine alkaloids. Incorporation of Δ^1 -piperidine into matrine. *Can. J. Chem.* **1981**, *59*, 106–115.

(12) Mandell, L.; Singh, K. P.; Gresham, J. T.; Freeman, W. Total synthesis of d,l-matrine. *J. Am. Chem. Soc.* **1963**, *85*, 2682–2683.

(13) Okuda, S.; Yoshimoto, M.; Tsuda, K. Studies on lupin alkaloids. IV. Total syntheses of optically active matrine and allomatrine. *Chem. Pharm. Bull.* **1966**, *14*, 275–279.

(14) Chen, J.; Browne, L. J.; Gonnella, N. C. Total synthesis of ($\pm$)-matrine. *J. Chem. Soc., Chem. Commun.* **1986**, 905–907.

(15) Boiteau, L.; Boivin, J.; Liard, A.; Quiclet-Sire, B.; Zard, S. Z. A short synthesis of ($\pm$)-matrine. *Angew. Chem., Int. Ed.* **1998**, *37*, 1128–1131.

(16) Shortly after the deposition of this work on ChemRxiv (DOI: 10.26434/chemrxiv-2022-0v94t), an elegant approach to the matrine alkaloids was disclosed: Magann, N. L.; Westley, E.; Sowden, M. J.; Gardiner, M. G.; Sherburn, M. S. Total synthesis of matrine alkaloids. *ChemRxiv* **2022**, DOI: 10.26434/chemrxiv-2022-j87g9. (accessed July 7, 2022).

(17) Watkin, S. V.; Camp, N. P.; Brown, R. C. D. Total synthesis of the tetracyclic lupin alkaloid (+)-allomatrine. *Org. Lett.* **2013**, *15*, 4596–4599.

(18) Lyu, X. Stereoselective total synthesis of lupin alkaloids. Ph.D. Dissertation, University of Southampton, Southampton, U.K., 2018. <https://eprints.soton.ac.uk/429608/> (accessed Feb. 15, 2022).

(19) There is precedent for the first step of this cascade cyclization, see: Warneke, J.; Plaumann, M.; Wang, Z.; Bohler, E.; Kemken, D.; Kelm, S.; Leibfritz, D.; Azov, V. A. *Tetrahedron Lett.* **2015**, *56*, 1124–1127.

(20) Ueno, A.; Morinaga, K.; Fukushima, S.; Iitaka, Y.; Koiso, Y.; Okuda, S. Studies on lupin alkaloids. VI. Isolation and structure of (+)-isomatrine. *Chem. Pharm. Bull.* **1975**, *23*, 2560–2566.

(21) Galasso, V.; Asaro, F.; Berti, F.; Pergolese, B.; Kovač, B.; Pichierri, F. On the molecular and electronic structure of matrine-type alkaloids. *Chem. Phys.* **2006**, *330*, 457–468.

(22) MilliporeSigma; Pyridine. Product No. P57506-4L (accessed June 16, 2022). Oakwood Chemical; Glutaryl chloride. Product No. 095828-100g (accessed June 16, 2022). Fischer Scientific; Dichloromethane. Product No. D37-20 (accessed June 16, 2022). Fischer Scientific; Methanol. Product No. A412SK-20 (accessed June 16, 2022).

(23) See [Supporting Information](#) for more details.

(24) Paull, D. H.; Weatherwax, A.; Lectka, T. Catalytic, asymmetric reactions of ketenes and ketene enolates. *Tetrahedron* **2009**, *65*, 6771–6803.

(25) Wink, M.; Hartmann, T.; Witte, L. Enzymatic synthesis of quinolizidine alkaloids in lupin chloroplasts. *Z. Naturforsch.* **1980**, *35*, 93–97.

(26) Grierson, D. The Polonovski reaction. *Org. React.* **1990**, *39*, 85–295.

(27) Kessar, S. V.; Singh, P.; Singh, P. K. N.; Singh, S. K. Facile α -deprotonation-electrophilic substitution of quinuclidine and DABCO. *Chem. Commun.* **1999**, 1927–1928.

(28) See [Tables S1–S4](#) in the Supporting Information.

(29) Chuang, T.-H.; Yang, C.-C.; Chang, C.-J.; Fang, J.-M. Base-catalyzed autoxidation of α -aminonitriles. An efficient method for conversion of aldehydes to amides and 2-amino-2-sulfonylacetonitrile to carbamates. *Synlett* **1990**, *1990*, 733–734.

(30) García-Valverde, M.; Pedrosa, R.; Vicente, M. A novel and efficient oxidation of 1,2-amino alcohols to dialkylamides. *Synlett* **2002**, *12*, 2092–2094.

(31) Ibragimov, B. T.; Tishchenko, G. N.; Kushmuradov, Yu. K.; Aripov, T. F.; Sadykov, A. S. Molecular and crystal structure of sophoridine. *Chem. Nat. Compd.* **1979**, *15*, 308–314.

(32) See [Table S20](#) in the Supporting Information for more details.

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