

A tosyliminium ion-based total synthesis of (\pm)-schefferine

Darío A. Bianchi and Teodoro S. Kaufman

Abstract: The synthesis of the phenolic tetrahydropprotoberberine alkaloid (\pm)-schefferine is reported, featuring as key steps a tosyliminium ion-mediated Friedel–Crafts alkylation of eugenol dimethyl ether and an intramolecular Mitsunobu-type amination.

Key words: total synthesis, (\pm)-schefferine, natural product, tosyliminium ion, Mitsunobu amination.

Résumé : On a réalisé la synthèse de la (\pm)-schefférine, un alcaloïde phénolique dérivé de la tétrahydropprotoberbérine. Les étapes clés de cette synthèse sont une alkylation de Friedel–Crafts l'éther diméthylé de l'eugénol assistée par l'ion tosyliminium et une amination intramoléculaire du type Mitsunobu.

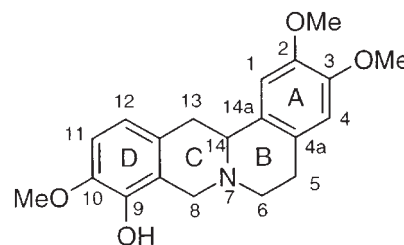
Mots clés : synthèse totale, (\pm)-schefférine, produit naturel, ion tosyliminium, amination de Mitsunobu.

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In 1972, Gellert and Rudzats (1) reported the isolation of schefferine from the bark of *Schefferomitra subaequalis* Diels (Anonaceae), a New Guinea liana found as a climber on rain forest trees. The structure of this phenolic tetrahydropprotoberberine alkaloid, also known as tetrahydropalmatrubine (2), was formulated as **1** on the basis of its ^1H NMR and mass spectral data.

Several syntheses of (\pm)-schefferine have been previously reported, including reduction of protoberberines as well as Mannich cyclization and photolysis of 1-substituted tetrahydroisoquinolines. Späth and Burger (3) prepared (\pm)-**1** long before its isolation from a natural source by reduction of palmatrubine, a monodemethylation product of the widely known alkaloid palmatine. A similar approach, involving the synthesis and reduction of a palmatrubine derivative, was followed by Dutta and Bradsher (2b).

More recently, Kametani and co-workers informed that the Mannich cyclization of a conveniently substituted 1-benzyltetrahydroisoquinoline under careful pH control, furnished moderate yields of (\pm)-schefferine (4a). The same group also reported the synthesis of this natural product employing the Mannich reaction of a brominated 1-benzyl tetrahydroisoquinoline, produced by a Bischler–Napieralski reaction (4b). Noteworthy, they were unable to obtain (\pm)-**1** by phenolic cyclization of a related substrate (4c).



(\pm)-Schefferine, (\pm)-**1**

In addition, (\pm)-schefferine was isolated as a minor product resulting from the Mannich reaction of a 1-benzyltetrahydroisoquinoline with formaldehyde generated in situ during the photolysis of the starting heterocycle (5). Interestingly, better yields of (\pm)-**1** were realized when photolysis of bromoenamides was employed as synthetic strategy (6).

Tracer experiments on *Stephania glabra* Miers (Menispermaceae) evidenced high incorporation of (\pm)-[aryl- ^3H]-schefferine into corydalmine but not into stepholidine, indicating that **1** might be a possible intermediate of the biosynthesis of corydalmine from reticuline (7a). Likewise, schefferine has been postulated as an intermediate in the biosynthesis of sinactine from reticuline (2a) and as a precursor of tetrahydropalmatine (7b).

We have reported a convenient entry to 3-substituted tetrahydroisoquinolines featuring the reaction of silicon-based nucleophiles with tosyliminium ions, generated upon addition of Lewis acids to tosylamidals (8). By capturing the tosyliminium ions with electron rich aromatics, such as phenols and their ethers, we recently extended the scope of this transformation to the elaboration of the very useful 3-aryl tetrahydroisoquinolines (9).

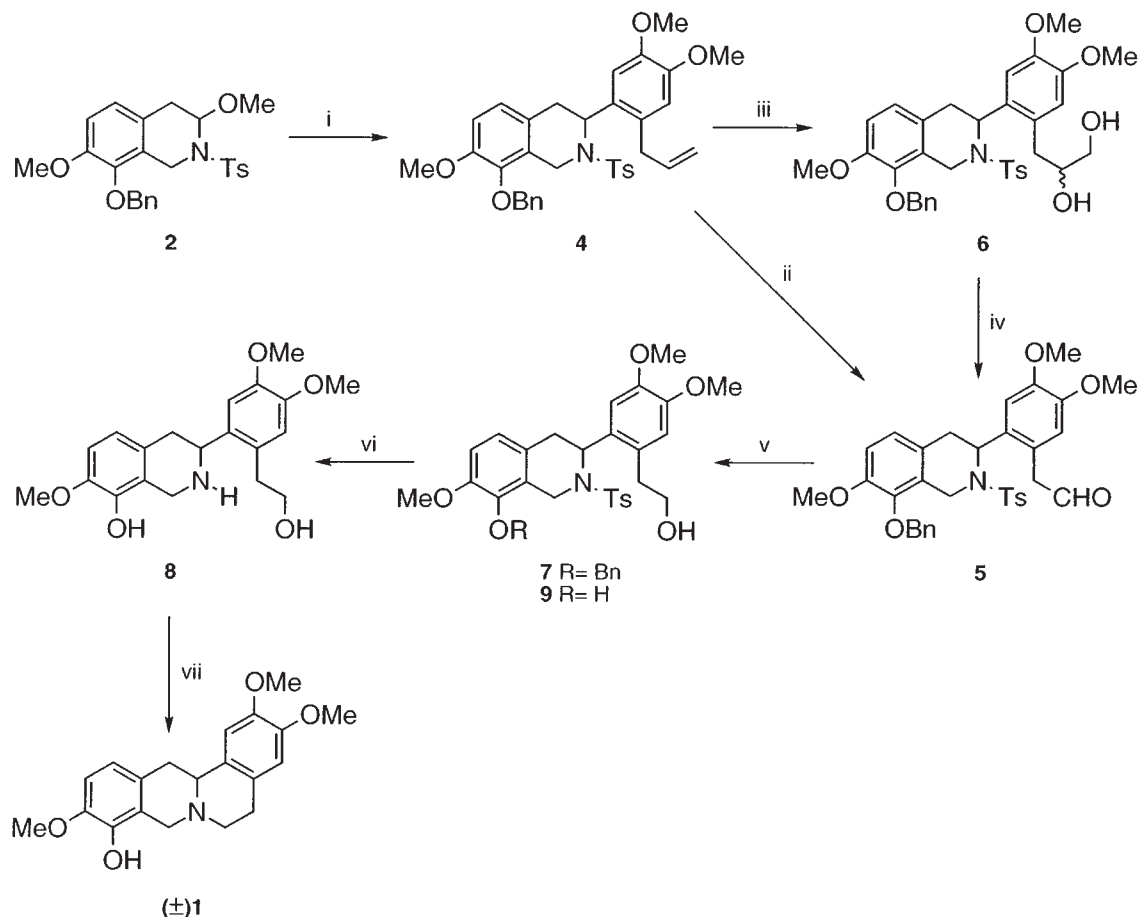
Herein, we disclose the details of a new and efficient total synthesis of (\pm)-schefferine via a new approach, consisting in the tosyliminium ion mediated preparation of a 3-aryl

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Scheme 1. Reagents and conditions: (i) 4-allyl-1,2-dimethoxybenzene (**3**), $\text{BF}_3 \cdot \text{Et}_2\text{O}$, CH_2Cl_2 , -78°C , 15 min, -30°C , 30 min; (ii) OsO_4 (cat.), NaIO_4 , $\text{THF-H}_2\text{O}$ (3:1); (iii) OsO_4 (cat.), NMO, $\text{Me}_2\text{CO-H}_2\text{O-BuOH}$ (4:2:1); (iv) NaIO_4 , $\text{THF-H}_2\text{O}$ (3:1); (v) NaBH_4 , $\text{MeOH-Et}_2\text{O}$ (4:1); (vi) (1) Na, NH_3 , -33°C ; (2) NH_4Cl , $-33^\circ\text{C} \rightarrow \text{rt}$; and (vii) PPh_3 , DEAD, HBF_4 , THF, reflux.



tetrahydroisoquinoline intermediate and a Mitsunobu-type intramolecular amination (10).

Although syntheses of alkaloids have made extensive use of acyliminium ion chemistry (11), the reactivity of the related tosyliminium ions has been comparatively less explored.

The known amide **2** (**8**) was treated at -78°C with the commercially available 4-allyl-1,2-dimethoxybenzene (**3**) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ to give the 3-aryl tetrahydroisoquinoline derivative **4** in 88% yield. β -Phenethyl alcohol **7** was then synthesized from **4** in two steps. First, sodium periodate-assisted oxidative olefin cleavage with osmium tetroxide as catalyst in THF-water (12) gave aldehyde **5** in 77% yield; then, reduction of aldehyde **5** with sodium borohydride in dry methanol furnished alcohol **7** in 92% yield.

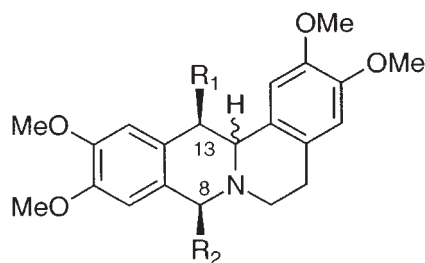
Because phenylacetaldehyde **5** tended to overoxidize, probably through its enol form, the dihydroxylation and oxidative fission steps were carried out separately, employing NMO as cooxidant during the dihydroxylation step, which resulted in an increased overall yield of 89%.

Debenzylation, desulfonylation, and formation of ring B were required to complete the synthesis. Our previous work suggested converting **7** into **8** by a stepwise process, consisting of catalytic debenzylation to yield phenol **9**, followed by sodium-mediated cleavage of the sulfonamide moiety. Although this approach allowed a better control of the delivery of the alkaline metal to the reaction medium to avoid forma-

tion of undesirable over-reduced side-products and furnish optimum yields of tetrahydroisoquinolines (**13**), reaction of **7** with sodium in liquid ammonia was found to cleanly effect simultaneous cleavage of both protective groups (14), providing amino alcohol **8** in 83% yield.

Finally, intramolecular Mitsunobu amination of **8** with the DEAD- PPh_3 couple in dry THF containing 1 equiv of HBF_4 gave 82% of (\pm)-schefferine [(\pm)-**1**], exhibiting a melting point and ^1H NMR spectrum identical with reported data (4b, 5b). The use of HBF_4 as additive was key for the success of this transformation to cyclized product in good yields. Protonation of the DEAD-derived hydrazide anion intermediate, is presumed to avoid its involvement as a competing nucleophile in the amination process (10b).

Dean and Rapoport (15) reported the syntheses of 8- and 13-methylberberines **10** and **11** by intramolecular cyclizations involving iminium ions formed by α -aminoacid decarbonylation. More recently, Padwa and Waterson (16) described a protoberberine synthesis which furnished **12**, employing a thionium- N -acyliminium ion cyclization of amido sulfoxides for the assembly of rings B and C. Unlike the above presented sequence leading to (\pm)-schefferine, these iminium ion-based synthetic strategies involved construction of ring B by formation of the $\text{C}_6\text{--N}$ bond prior to the elaboration of the $\text{C}_{14}\text{--C}_{14a}$ bond between rings A and C. The scope and limitations of this alternative protocol are currently



10 $R_1 = \text{H}, R_2 = \text{Me}$
11 $R_1 = \text{Me}, R_2 = \text{H}$

being evaluated for the synthesis of protoberberine-type natural products.

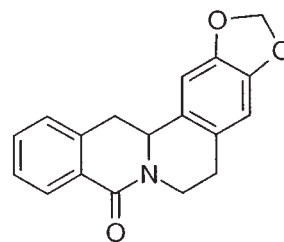
Experimental section

Melting points were measured on an Ernst Leitz hot-stage microscope apparatus and are uncorrected. IR spectra were taken on a Beckman Acculab 8 spectrophotometer with solid samples as KBr pellets and liquid samples as films. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 , on a Bruker AC-200E instrument at 200.13 and 50.33 MHz respectively, with TMS as the internal standard. ^{13}C NMR resonances corresponding to two carbon atoms are designated with an asterisk while those assigned to three carbons are marked with "#." High resolution mass spectra were obtained from UMYMFOR (FCEN, Buenos Aires).

4-Allyl-1,2-dimethoxybenzene was purchased from Aldrich Chemical Co. and used without further purification. All reactions were carried out in a dry oxygen-free nitrogen atmosphere, monitored by thin layer chromatography on Merck's precoated silica gel 60 F_{254} TLC plates developed in hexane–EtOAc (7:3) or CHCl_3 –EtOH (8:2) and detected by examination under UV light followed by spraying with 2% *p*-anisaldehyde–sulfuric acid reagent in EtOH or 0.2% ninhydrin in EtOH. Careful heating improved the sensitivity of the detection. All new compounds gave a single spot by TLC. Flash chromatography was carried out on Merck Kieselgel 60 (0.04–0.063 mm), packed in hexane; elution was with mixtures of hexane–EtOAc, using gradient techniques. Compounds were preadsorbed from Et_2O or CH_2Cl_2 solutions onto the adsorbent before column chromatography.

3-(2-Allyl-4,5-dimethoxyphenyl)-8-benzyloxy-7-methoxy-2-(toluene-4-sulfonyl)-1,2,3,4-tetrahydroisoquinoline (**4**)

A CH_2Cl_2 solution of 4-allyl-1,2-dimethoxybenzene (0.88 mL, 0.49 mmol) was added to amidal **2** (110 mg, 0.243 mmol) in anhydrous CH_2Cl_2 (3 mL) and the resulting solution was cooled to -78°C . Then, a solution of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in CH_2Cl_2 (0.51 mL, 0.29 mmol) was added dropwise. Stirring continued for 15 min at -78°C and 30 min at -30°C . Then the reaction mixture was rapidly poured over brine (10 mL) and the products were extracted with EtOAc (4 \times 25 mL). Drying (Na_2SO_4), concentration, and chromatography of the combined ethereal extracts afforded the 3-aryl-tetrahydroisoquinoline derivative **4** (128 mg, 88%) as a colourless oil which crystallized on standing, mp 120 – 121.5°C (hexane–EtOAc). IR (neat) (cm^{-1}): 2920, 2850,



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1600, 1500, 1440, 1350, 1280, 1160, 1070, 910, 820, 730, and 660. ^1H NMR δ : 2.41 (s, 3H), 2.79 (dd, $J = 9.0$, 11.8 Hz, 1H), 3.36 (brd, 2H), 3.60 (s, 3H), 3.68 (dd, $J = 5.4$, 11.8 Hz, 1H), 3.85 (s, 3H), 3.87 (s, 3H), 3.89 (d, $J = 15.9$ Hz, 1H), 4.38 (dd, $J = 5.4$, 9.0 Hz, 1H), 4.55 (d, $J = 15.9$ Hz, 1H), 4.93–5.10 (m, 2H), 5.03 (d, $J = 11.1$ Hz, 1H), 5.12 (d, $J = 11.1$ Hz, 1H), 5.85–6.06 (m, 1H), 6.23 (s, 1H), 6.48 (d, $J = 8.7$ Hz, 1H), 6.68 (s, 1H), 6.71 (d, $J = 8.7$ Hz, 1H), 7.25 (d, $J = 8.2$ Hz, 2H), 7.30–7.50 (m, 5H) and 7.57 (d, $J = 8.2$ Hz, 2H). ^{13}C NMR δ : 21.37, 36.91, 39.77, 44.31, 49.89, 55.69, * 55.81, 74.22, 111.20, 112.42, 112.71, 115.79, 124.39, 126.77, 127.49, * 127.97, # 128.25, * 129.47, * 130.11, 130.22, 132.34, 133.57, 137.32, 137.42, 143.28, * 147.24, 147.62, and 150.25. HREIMS calcd. for $\text{C}_{35}\text{H}_{37}\text{NO}_6\text{S}$: 599.2342; found: 599.2347.

2-{2-[8-Benzyloxy-7-methoxy-2-(toluene-4-sulfonyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]-4,5-dimethoxyphenyl}-ethanol (**7**)

A 2% w/v solution of OsO_4 in *tert*-butanol (0.051 mL) was added to a mixture of allyl tetrahydroisoquinoline **4** (125 mg, 0.21 mmol) and potassium periodate (144 mg, 0.63 mmol) in 3:1 THF–water (4 mL). The mixture was stirred overnight at room temperature and quenched with 10% sodium hydrogensulfite (5 mL); Celite (1 g) was added and stirring continued for an additional 1 h, then the suspension was filtered under reduced pressure through Celite contained in a Büchner funnel and the crude reaction product was exhaustively extracted with EtOAc (5 \times 20 mL). The organic portion was dried (Na_2SO_4), concentrated, and chromatographed to furnish aldehyde **5** (96 mg, 77%) as an oil. IR (neat) (cm^{-1}): 2960, 2870, 1750, 1630, 1510, 1480, 1380, 1300, 1190, 1090, 970, 840, 760, and 680. ^1H NMR δ : 2.42 (s, 3H), 2.83 (dd, $J = 8.5$, 11.9 Hz, 1H), 3.55–3.75 (m, 3H), 3.60 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 3.93 (d, $J = 16.5$ Hz, 1H), 4.22 (dd, $J = 5.0$, 8.5 Hz, 1H), 4.47 (d, $J = 16.5$ Hz, 1H), 5.03 (d, $J = 11.2$ Hz, 1H), 5.13 (d, $J = 11.2$ Hz, 1H), 6.34 (s, 1H), 6.52 (d, $J = 8.6$ Hz, 1H), 6.63 (s, 1H), 6.72 (d, $J = 8.6$ Hz, 1H), 7.25 (d, $J = 8.3$ Hz, 2H), 7.35–7.52 (m, 5H), 7.58 (d, $J = 8.3$ Hz, 2H) and 9.70 (s, 1H). ^{13}C NMR δ : 21.32, 40.46, 44.22, 47.64, 49.72, 55.62, 55.72, * 74.16, 111.28, 112.80, 113.41, 122.17, 124.36, 126.61, 127.38, * 127.96, 128.24 (4 carbons), 129.33, 129.49, * 133.41, 133.56, 137.28, 143.18, 143.39, 147.86, 148.19, 150.39, and 198.74. HREIMS calcd. for $\text{C}_{34}\text{H}_{35}\text{NO}_7\text{S}$: 601.2134; found: 601.2132.

Without further purification, aldehyde **5** (66 mg, 0.11 mmol) was dissolved in a 4:1 MeOH– Et_2O mixture (10 mL) kept at 0°C in an ice water bath. Sodium

borohydride (10 mg, 0.26 mmol) was added, stirring continued during 15 min and the reaction was quenched with 10% w/v citric acid solution (10 mL). The organic solvent was evaporated under reduced pressure and the reaction product was extracted with EtOAc (4 × 15 mL). The organic extract was dried (Na₂SO₄), concentrated under reduced pressure, and the glassy residue was chromatographed, yielding alcohol **7** (61 mg, 92%), as a solid, mp 148–149.5°C. IR (KBr) (cm⁻¹): 3520, 2960, 2860, 1620, 1530, 1480, 1370, 1310, 1190, 1090, 980, 830, 760, and 680. ¹H NMR δ: 1.90 (brs, *w*_{1/2} = 13 Hz, 1H), 2.40 (s, 3H), 2.84 (dd, *J* = 7.4, 10.2 Hz, 1H), 2.88–3.02 (m, 2H), 3.59 (s, 3H), 3.69 (dd, *J* = 4.5, 10.2 Hz, 1H), 3.76–3.90 (m, 2H), 3.84 (s, 3H), 3.87 (s, 3H), 3.91 (d, *J* = 15.9 Hz, 1H), 4.43 (dd, *J* = 4.5, 7.4 Hz, 1H), 4.55 (d, *J* = 15.9 Hz, 1H), 5.03 (d, *J* = 11.2 Hz, 1H), 5.12 (d, *J* = 11.2 Hz, 1H), 6.22 (s, 1H), 6.48 (d, *J* = 8.6 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 6.74 (s, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.30–7.51 (m, 5H) and 7.58 (d, *J* = 8.2 Hz, 2H). ¹³C NMR δ: 21.34, 35.69, 39.60, 44.32, 50.14, 55.64, * 55.77, 63.60, 74.18, 111.16, 112.23, 112.76, 124.35, 126.73, 127.39, * 127.95, 128.20, * 128.25, * 129.04, 129.48, * 130.11, 132.61, 133.54, 137.37, 143.24, 143.33, 147.38, 147.59, and 150.25. HREIMS calcd. for C₃₄H₃₇NO₇S: 603.2291; found: 603.2287.

2-{2-[8-Benzyloxy-7-methoxy-2-(toluene-4-sulfonyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]-4,5-dimethoxyphenyl}-acetaldehyde (5**)**

A 2% w/v solution of OsO₄ in *tert*-butanol (0.100 mL) was added to a mixture of allyl tetrahydroisoquinoline **4** (250 mg, 0.42 mmol) and NMO (103 mg, 0.88 mmol) in 4:2:1 acetone–water–*tert*-butanol (8 mL). The mixture was stirred overnight at room temperature and then quenched with 10% sodium hydrogensulfite (5 mL). Celite (1 g) was added and stirring continued for an additional 1 h, when the suspension was filtered under reduced pressure through Celite contained in a Büchner funnel and the crude reaction product was exhaustively extracted with EtOAc (5 × 20 mL). The organic portion was dried (Na₂SO₄) and concentrated to yield **6**, as an oily 1:1 epimeric mixture (251 mg, 95%). IR (film) (cm⁻¹): 3450, 2950, 2860, 1600, 1500, 1290, 1190, 1070, 920, and 740. Without further purification, the mixture of diols (125 mg) was dissolved in 3:1 THF–water (4 mL) and treated with sodium periodate (101 mg, 0.44 mmol). The reaction was stirred 2 h at room temperature, then it was diluted with brine (5 mL) and extracted with EtOAc (5 × 20 mL). The combined organic extracts were dried (Na₂SO₄), concentrated in vacuum, and chromatographed, providing aldehyde **5** (111 mg, 94%) as an oil.

3-[2-(2-Hydroxyethyl)-4,5-dimethoxyphenyl]-8-hydroxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (8**)**

Anhydrous ammonia (10 mL) was condensed in a three-necked flask, fitted with a dry ice – acetone condenser protected with a calcium chloride tube and an ammonia inlet, and containing sulfonamide **7** (50 mg, 0.083 mmol) dissolved in dry THF (3 mL). With rapid stirring, sodium metal contained in a graduated glass tube was added portionwise to the reaction mixture until the characteristic blue colour persisted for 10 min. The reaction was quenched with ammonium chloride (50 mg) and MeOH (2 mL). The ammonia

was slowly evaporated and the reaction products were mixed with silica gel. The solvent was removed under reduced pressure and the adsorbed reaction products were chromatographed (CH₂Cl₂–EtOH), furnishing **8** (25 mg, 83%) as an oil. IR (neat) (cm⁻¹): 3550–2500, 2960, 2880, 1630, 1500, 1470, 1280, 1060, 920, and 740. ¹H NMR δ: 2.91 (dd, *J* = 8.8, 12.3 Hz, 1H), 2.94 (brd, 2H), 3.31 (dd, *J* = 5.2, 12.3 Hz, 1H), 3.64 (s, 3H), 3.75–3.92 (m, 1H), 3.80 (s, 3H), 3.86 (s, 3H), 4.00–4.30 (m, 6H), 4.35 (dd, *J* = 5.2, 8.8 Hz, 1H), 6.25 (d, *J* = 8.5 Hz, 1H), 6.34 (s, 1H), 6.59 (d, *J* = 8.5 Hz, 1H) and 6.72 (s, 1H). ¹³C NMR δ: 35.99, 39.31, 43.09, 50.76, 55.72, 55.77, 55.85, 63.62, 106.92, 112.18, 112.84, 119.97, 121.75, 129.17, 131.31, 134.07, 141.37, 144.17, 147.31, and 147.42. HREIMS calcd. for C₂₀H₂₅NO₅: 359.1733; found: 359.1736.

(±)-2,3,10-Trimethoxy-9-hydroxy-5,6,13,13a-tetrahydro-8H-dibenzo[*a,g*]quinolizine ((±)-schefferine, (±)-1**)**

Diethyl azodicarboxylate (0.022 mL, 0.122 mmol) was added all at once to a stirred solution of **8** (22 mg, 0.061 mmol), triphenylphosphine (32 mg, 0.122 mmol), and ethereal HBF₄ (0.008 mL, 0.067 mmol) in THF (2 mL). The reaction was stirred under reflux until complete conversion of the aminoalcohol was assessed by TLC; then, the volatiles were removed under reduced pressure and the remaining oil was chromatographed, yielding (±)-**1** (17 mg, 82%) as a solid, mp 146.5–148°C (lit. (5*b*) 144–145°C and (4*b*) 147–148°C). IR (KBr) (cm⁻¹): 3430, 2930, 2850, 2800–2720, 1630, 1590, 1500, 1450, 1340, 1290, 1200, 1140, 1070, 990, and 740. ¹H NMR δ: 2.18 (dd, *J* = 3.8, 13.3 Hz, 1H), 3.03 (dd, *J* = 2.3, 13.3 Hz, 1H), 3.18–3.56 (m, 5H), 3.68 (brs, 1H), 3.80 (s, 3H), 3.84 (s, 3H), 3.93 (s, 3H), 4.16 (d, *J* = 17.8 Hz, 1H), 4.33 (d, *J* = 17.8 Hz, 1H), 6.49 (s, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 1H) and 6.82 (s, 1H). ¹³C NMR δ: 34.15, 43.39, 48.42, 52.19, 55.76, 55.90, 56.06, 56.13, 108.89, 112.96, 114.36, 120.69, 121.95, 129.25, 133.09, 137.89, 140.49, 143.93, 146.45, and 146.51. HREIMS calcd. for C₂₀H₂₃NO₄: 341.1627; found: 341.1622.

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References

1. E. Gellert and R. Rudzats. *Aust. J. Chem.* **25**, 2477 (1972).
2. (a) D.S. Bhakuni, S. Jain, and S. Gupta. *Tetrahedron*, **39**, 455 (1983); (b) N.L. Dutta and C.K. Bradsher. *J. Org. Chem.* **27**, 2213 (1962).
3. E. Späth and G. Burger. *Ber. Dtsch. Chem. Ges.* **59**, 1486 (1926).
4. (a) S.F. Dyke. The isoquinoline alkaloids. In *Rodd's chemistry of carbon compounds*. Vol. IV H. 2nd ed. Edited by S. Coffey. Elsevier, New York, 1978. p. 132; (b) T. Kametani, M. Ihara, and T. Honda. *J. Chem. Soc. C* 1060 (1970); (c) T. Kametani, K. Fukumoto, H. Agui, H. Yagi, K. Kigasawa, H. Sugahara, M. Hiragi, T. Hayasaka, and H. Ishimaru. *J. Chem. Soc. C* 112 (1968).
5. (a) T.R. Govindachari, K. Nagarajan, S. Rajeswari, H. Suguna, and B.R. Pai. *Indian J. Chem. Sect. B: Org. Chem. Incl. Med.*

- Chem. **15B**, 873 (1977); (b) T. Kametani, K. Fukumoto, M. Ihara, M. Takemura, H. Matsumoto, B.R. Pai, K. Nagarajan, M.S. Premila, and H. Suguna. *Heterocycles*, **3**, 811 (1975).
6. T. Kametani, T. Sugai, Y. Shoji, T. Honda, F. Sato, and K. Fukumoto. *J. Chem. Soc. Perkin Trans. 1*, 1151 (1977).
7. (a) D.S. Bhakuni, S. Gupta, and S. Jain. *Tetrahedron*, **39**, 4003 (1983); (b) D.S. Bhakuni, S. Jain, and S. Gupta. *Tetrahedron*, **36**, 2491 (1980).
8. V.L. Ponzio and T.S. Kaufman. *Synlett*, 1149 (1995).
9. D.A. Bianchi and T.S. Kaufman. *Synlett*, 801 (2000).
10. (a) R.C. Bernotas and R.V. Cube. *Tetrahedron Lett.* **32**, 161 (1991); (b) P.G. Sammes and S. Smith. *J. Chem. Soc. Perkin Trans. 1*, 2415 (1984).
11. H. Hiemstra and W.N. Speckamp. Additions to *N*-acyliminium ions. In *Comprehensive organic synthesis*. Vol. 2. Edited by B.M. Tost and I. Fleming. Pergamon Press, New York. 1991. pp. 1047–1082.
12. E.J. Corey, R.L. Danheiser, S. Chandrasekaran, P. Siret, G.E. Keck, and J.L. Gras. *J. Am. Chem. Soc.* **100**, 8031 (1978).
13. T.S. Kaufman. *J. Chem. Soc. Perkin Trans. 1*, 403 (1993).
14. K. Ito and H. Tanaka. *Chem. Pharm. Bull.* **25**, 1732 (1977).
15. R.T. Dean and H. Rapoport. *J. Org. Chem.* **43**, 4183 (1978).
16. A. Padwa and A. G. Waterson. *Tetrahedron Lett.* **39**, 8585 (1998).