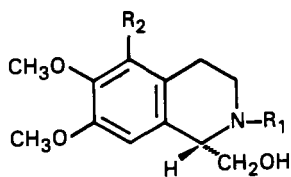


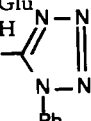
ABSOLUTE CONFIGURATION OF DEGLUCOPTEROCEREINE:
CONVERSION INTO *R*-(+)-*N*-METHYLCALYCOTOMINE¹P. KERÉKES,² PADAM N. SHARMA,³ A. BROSSI,*Medicinal Chemistry Section, Laboratory of Chemistry, National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20205*

and J.L. McLAUGHLIN

Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, Indiana 47907

Pterocereine (**1**), a glucotetrahydro-isoquinoline alkaloid from the cactus *Pterocereus gaumeri* (Br. & R.) MacDoug. & Mir., afforded by hydrolysis deglucopterocereine (**2**) of unknown absolute configuration (1). Phenolic deoxygenation (2) of **2** by reductive cleavage of its phenyltetrazolyl ether derivative (**3**) has afforded *R*-(+)-*N*-methylcalycotomine (**4**). Identity of **4** with material prepared from *R*-(+)-calycotomine (**5**) (3) by reductive *N*-methylation (4) was established by tlc and a comparison of mass and cd-spectra of **4** obtained from **2** and **5**. Thus, the *R*-configuration of deglucopterocereine (**2**) was established. Furthermore, optical characterization can be carried out by cd spectroscopy with only small amounts (1 mg or less) of materials (**5**).



- 1** $R_1 = \text{CH}_3$, $R_2 = \text{OGlu}$
2 $R_1 = \text{CH}_3$, $R_2 = \text{OH}$
3 $R_1 = \text{CH}_3$, $R_2 = \text{O}$ —
4 $R_1 = \text{CH}_3$, $R_2 = \text{H}$
5 $R_1 = R_2 = \text{H}$

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded with a Beckman 4230 instrument. Nmr spectra were obtained in CDCl_3 with a Varian HR-220 spectrometer with TMS as an internal standard. Cims spectra were obtained by using a Finnigan 1015 D spectrometer. Cd-spectra were measured in MeOH solution at 283 nm with a J-500A spectropolarimeter (Φ = molecular rotation). Tlc was carried out on silica gel plates, purchased from Analtech, Inc., developed with CHCl_3 -MeOH- NH_4OH (94:5:1).

CONVERSION OF DEGLUCOPTEROCEREINE (**1**) INTO (+)-*N*-METHYLCALYCOTOMINE (**2**).—A mixture of **1** hydrochloride (20 mg), 5-chloro-1-phenyl-1*H*-tetrazole (14.5 mg), and K_2CO_3 (38.7 mg) in Me_2CO (20 ml) was refluxed for 24 h. Evaporation to dryness, addition of H_2O (20 ml) and a few drops of 10% NH_4OH afforded, after extraction with CHCl_3 (3×20 ml) and usual workup, 20 mg of an oily residue. Column chromatography on silica gel (CHCl_3 -MeOH- NH_4OH , 90:10:1) gave 8.5 mg of the amorphous tetrazolyl ether **3**: cims m/z 398 ($M^+ + 1$). Hydrogenation of **3** (8.0 mg) in EtOH (10 ml) over 10% Pd/C-catalyst (10 mg) at 50° and 48 psi for 14 h afforded, after usual workup, 2.1 mg of an oil: cims m/z 238 ($M^+ + 1$), 206 ($M^+ - \text{CH}_2\text{OH}$); Cd Φ (λ nm) = -30.21° (283). Identical by tlc with (+)-*N*-methylcalycotomine (**4**).

(+)-*N*-METHYLCALYCOTOMINE (**4**) FROM (+)-CALYCOTOMINE (**5**).—(+)-Calycotomine (111 mg), $[\alpha]^{30\text{D}} = +23^\circ$ ($c=1$, MeOH) [lit. (2) $[\alpha]^{24\text{D}} = +24^\circ$ ($c=0.5$, MeOH)], prepared from its tartrate salt was dissolved in MeOH (0.5 ml), and 37% aqueous formaldehyde (0.06 ml) was added. After standing for 2 h at room temperature, NaCNBH_3 (65 mg) was added in small portions, and the reaction mixture was left standing overnight. Workup afforded an oily residue that was purified by chromatography on silica gel plates. The oily base (60 mg), eluted with the solvent mixture CHCl_3 -MeOH- NH_4OH (94:5:1) showed the following properties: $[\alpha]_{\text{D}} +55^\circ$ (c

¹Paper no. 60 in the series "Cactus Alkaloids,"²Dedicated to Dr. Peter Kerekes, a Visiting Scientist at the NIH from the Institute of Organic Chemistry, University of Debrecen, Hungary, who died on July 31, 1984, from a heart attack.³Department of Medicinal Chemistry, School of Pharmacy, University of Kansas, Lawrence, Kansas 66045.

0.4, CHCl₃); cims *m/z* 238 (M⁺ + 1), 206 (M⁺ - CH₂OH); ¹H nmr (CDCl₃) 6.57 (s, 1H, ArH), 6.53 (s, 1H, ArH), 3.83 (s, 6H, 2 OCH₃), 3.75 (m, 1H, C₁-H), 3.52 (m, 2H, CH₂OH), 3.12 (m, 2H, CH₂), 2.82 (m, 2H, CH₂), and 2.51 (s, 3H, NCH₃); ir (neat) 3400 (OH) and 1610 (aromatic) cm⁻¹; cd Φ (λ nm) = -30.28° (283); picrate mp 205° (dec).

ACKNOWLEDGMENTS

We thank Dr. H. Bruderer from the Research Division of F. Hoffmann-La Roche & Co., AG in Basel for a sample of (+)-calycotomine tartrate and a sample of natural (+)-calycotomine. Support from BMRG 507-RRO-5586 from NIH is acknowledged.

LITERATURE CITED

1. Y.A.H. Mohamed, C.J. Chang, and J.L. McLaughlin, *J. Nat. Prod.*, **42**, 197 (1979).
2. A. Brossi, M.F. Rahman, and K.C. Rice, *Heterocycles*, **7**, 277 (1977).
3. A. Brossi and H. Burkhardt, *Helv. Chim. Acta*, **44**, 1558 (1961).
4. K. Takahashi and A. Brossi, *Heterocycles*, **19**, 691 (1983).
5. K. Nakanishi, Plenary lecture at the 14th IUPAC Conference, July 9-14, Poznań, Poland, 1984.

Received 30 August 1984