which in turn may be converted into cularine- or turkiyenine[16]-type alkaloids, depending upon the enzymatic systems available in the plant.

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(16) Gözler, T.; Gözler, B.; Weiss, I.; Freyer, A. J.; Shamma, M. *J. Am. Chem. Soc.*, following paper in this issue.

(+)-Turkiyenine: An Unusual Extension of the Biogenetic Sequence for the Isoquinoline Alkaloids

Tekant Gözler

Department of Pharmacognosy, Faculty of Pharmacy Ege University, Bornova, Izmir, Turkey

Belkis Gözler

Department of Pharmaceutical Chemistry Faculty of Pharmacy, Ege University Bornova, Izmir, Turkey

Inge Weiss, Alan J. Freyer, and Maurice Shamma*

Department of Chemistry The Pennsylvania State University University Park, Pennsylvania 16802

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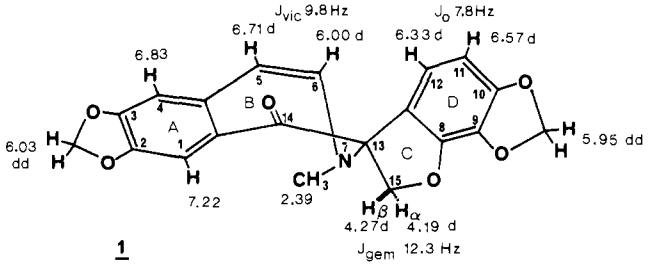
The amorphous base turkiyenine (**1**) was originally isolated by us 2 years ago, shortly following collection of the plant *Hypecoum procumbens* L. (Papaveraceae) in April 1982, near the village of Fethiye, in the province of Muğla, in south central Anatolia. Our original studies indicated that the alkaloid $C_{20}H_{15}NO_6$ ($[\alpha]^{23}_D$ +72° (*c* 0.053, $CHCl_3$); ν_{max} $CHCl_3$ 1663, 1710 cm^{-1}; λ_{max} MeOH 218 sh, 258, 281 sh, 352 nm (log ϵ 4.42, 4.62, 4.11, 3.55))[1] incorporated an *N*-methyl group, a ketonic function, a cis-disubstituted double bond as part of a seven-membered ring, and a spiro linkage—an amalgam of structural features hitherto unknown among the recognized isoquinoline- or isoquinoline-derived alkaloids.

In order to confirm the authenticity of (+)-turkiyenine (**1**) as an alkaloid, *H. procumbens* was collected again in 1983, on the same day and the same location where it had been gathered the previous year.[2] Extraction again provided (+)-turkiyenine, at which point a detailed structural study became warranted.



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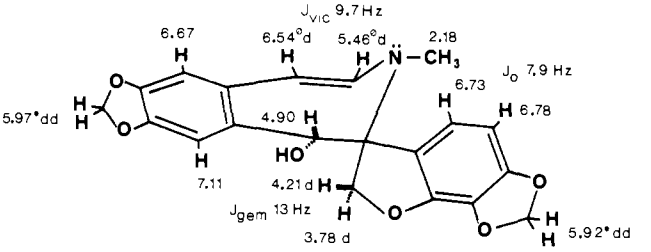
The 360-MHz (CD_3CN) ^1H NMR spectrum of turkiyenine has been summarized around expression **1** of relative configuration.[3] One *N*-methyl singlet is present at δ 2.39. Two methylenedioxy groups appear each as closely packed doublets of doublets, one set at δ 6.03 and the order at 5.95. The vinylic protons of the cisoid double bond are found at δ6.00 and 6.71, each as a doublet with J_{vic} = 9.8 Hz. A particularly informative feature of the spectrum was the two-proton methylene doublets at δ 4.19 and 4.27, J_{gem} = 12.3 Hz. A coupling of this magnitude is characteristic of a five-membered ring containing an oxygen atom.[4]

NMR NOEDS[5] proved to be particularly effective not only in the gross structural elucidation but also in the establishment of the favored conformation. The seven-membered ring is in a quasi-boat conformation. Irradiation of the *N*-methyl singlet (δ 2.39) caused enhancements of three signals, namely, H-1 (δ 7.22) by 3.0%, H-6 (δ 6.00) by 15%, and H-15α,β (δ 4.19–4.27) by ~5%. Irradiation of the methylenedioxy protons at δ 6.03 resulted in a 2.6% NOE of the H-1 (δ 7.22) singlet which has a long T_1 since no other proton is situated in its immediate vicinity. It follows that the alternate methylenedioxy absorption at δ 5.95 can be assigned to the substituent on ring D. A significant negative NOE of 2.6% was recorded for H-4 (δ 6.83) upon irradiation of the H-6 signal (δ 6.00).[6] This is a counterpoint to the strongly positive NOE of 19.4% observed for H-5 (δ 6.71) upon irradiation of H-6. Finally, by use of Gaussian multiplication, long-range coupling through five bonds could be detected between H-1 (δ 7.22) and H-5 (δ 6.71).

Reduction of (+)-turkiyenine (**1**) with sodium borohydride in methanol provided two amorphous alcohols, **2** and **3**, $C_{20}H_{17}NO_6$, in a 2:1 ratio. In both alcohols, the C-14 hydroxyl prefers to adopt



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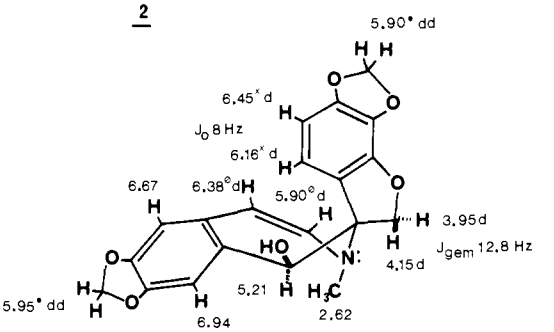

3 $J_{5,6}$ 9.8 Hz

a pseudoequatorial position. For the major compound **2**, $[\alpha]^{23}_D$ −28° (*c* 0.001, $CHCl_3$), two NMR NOE's were observed upon irradiation of the pseudoaxial H-14 at δ 4.90, viz., H-1 (δ 7.11)

(1) Turkiyenine: mass spectrum, *m/z* 364 (M − 1)$^+$ (0.9), 363 (6), 362 (18), 350 (14), 349 (59), 332 (54), 320 (100); CD Δε (nm) (MeOH) +1.2 (403), −9.5 (353), −2.4 (290), +22.4 (258), −10.1 (239).

(2) Plant collection dates were April 8, 1982 and 1983. The dried plant material (1.35 kg) was extracted with ethanol at room temperature. The usual acid–base workup, followed by silica gel chromatography, provided 30 mg of turkiyenine.

(3) We have found that CD_3CN is generally a superior solvent to $CDCl_3$ for recording the NMR spectra of alkaloids. The aromatic proton peaks are better separated, and the solvent is not as destructive of alkaloids as chloroform.

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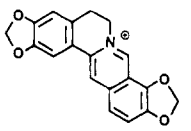
by 2.9% and H-12 (δ 6.73) by 15.3%. The latter NOE was critical in confirming that the ring-D methylenedioxy was located at C-9,10 rather than at the alternate C-11,12 site. Turning now to the minor compound **3**, $[\alpha]^{23}_D$ +409° (c 0.0007, $CHCl_3$), four NOE's were recorded following irradiation of the pseudoaxial H-14. The stronger two concerned the acidic C-14 alcoholic hydrogen at δ 3.12 (10.7%) and the N-methyl singlet at δ 2.62 (7.1%). Weaker effects were observed for the H-1 singlet at δ 6.94 (3.5%) and the H-15β doublet at δ4.15 (0.9%).[7]

The biogenesis of (+)-turkiyenine (**1**) appears to be radically different from that of any other isoquinoline-derived alkaloid. The origin of turkiyenine may hypothetically be traced to the pseudobenzylisoquinoline **5** which could be obtained biogenetically from the protoberberinium alkaloid coptisine (**4**).[8] Hydrolysis and



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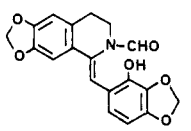

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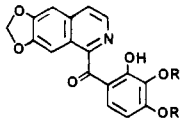
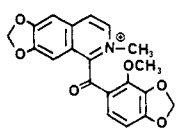


6a R+R=CH_2
6b R=CH_3



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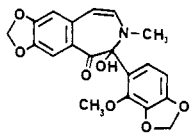

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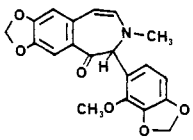

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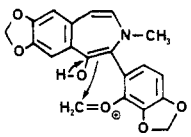

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oxidation of **5** would yield pseudobenzylisoquinoline **6a**, structurally related to the known rugosinone (**6b**).[9] O,N-Dimethylation of **6a** would provide salt **7**, which through base-catalyzed isomerization could lead to pseudobase **8**. Reduction of **8** would give rise to ketone **9**. Enolization of this ketone, and oxidation of the aromatic methoxyl group to an oxonium ion as in **10**, would then set the stage for the formation of the methylenoxy bridge[10] and the alkaloid (+)-turkiyenine (**1**).

It has been previously suggested that the intermediacy of pseudobenzylisoquinolines could be one of several possible ways by which 8,9,10-oxygenated aporphines may be formed in nature.[8] It is now apparent that pseudobenzylisoquinolines may also be implicated in the biogenesis of the unusual base (+)-turkiyenine (**1**).

Acknowledgment. This research was supported by NSF Grant CHE-8210699.

(7) (-)-Dihydroturkiyenine (**2**): ν_{max} ($CHCl_3$) 3350 cm^{-1}; λ_{max} MeOH 223, 288, 309 sh, 319 nm (log ϵ 4.47, 3.92, 3.83, 3.76); MS, m/z 365 $(M-2)^+$ (0.4), 364 (0.4), 351 (49), 323 (45), 322 (96), 320 (100), 308 (87). (+)-Epidihydroturkiyenine (**3**): ν_{max} ($CHCl_3$) 3550 cm^{-1}; λ_{max} MeOH 226, 286, 313 nm (log ϵ 4.44, 3.86, 3.79); MS, m/z 365 $(M-2)^+$ (0.3), 363 (0.3), 362 (1), 323 (46), 322 (100), 320 (47), 308 (96). NMR spectra for **2** and **3** are in CD_3CN.

(8) Pseudobenzylisoquinolines always incorporate three oxygenated substituents in the lower pendant aromatic ring and are possibly derived in the plant from the oxidation of protoberberinium salts. See: Murugesan, N.; Shamma, M. *Tetrahedron Lett.* **1979**, 4521. Shamma, M.; Guinaudeau, H. *Tetrahedron*, in press.

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Synthesis and DNA Binding and Photonicking Properties of Acridine Orange Linked by a Polymethylene Tether to (1,2-Diaminoethane)dichloroplatinum(II)

Bruce E. Bowler, L. Steven Hollis, and Stephen J. Lippard*

Departments of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
and Columbia University
New York, New York 10027

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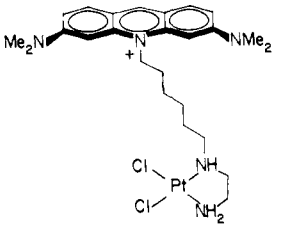
There is much current interest in the binding of the antitumor drug *cis*-diamminedichloroplatinum(II) (*cis*-DDP) to its putative target in the cancer cell, DNA.[1] Both the position and mode of binding of *cis*-DDP to DNA can be altered by the presence of the intercalating dye ethidium bromide in the incubation medium.[2] Moreover, prior coordination of *cis*-DDP or $[Pt(en)Cl_2]$ (en = 1,2-diaminoethane) is known to affect the binding of intercalators to DNA.[3] We were therefore interested to construct a molecule in which both an intercalating functionality and a diamine-coordinated $\{PtCl_2\}$ moiety are connected by an appropriate linker chain and to study its DNA binding and cleaving properties. There is precedence for compounds containing both intercalator and metal-binding functionalities in the naturally occurring antitumor antibiotic bleomycin,[4] in a family of synthetic molecules designed as footprinting agents,[5] and in certain metallointercalation reagents such as [Pt(terpy)Cl]Cl.[3a] Here we report the synthesis, characterization, DNA binding, and photoactivated DNA cleaving (nicking) properties of cation **1**, in which acridine orange is linked by a hexamethylene chain to (1,2-diaminoethane)dichloroplatinum(II).

Compound **1** was synthesized in overall 18% yield by the following nine-step procedure. The hydroxyl group of 6-chloro-1-



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hydroxyhexane was protected with dihydropyran,[6] following which the chloro group was converted to an iodo group by a Finkelstein reaction.[7] Alkylation of acridine orange free base[8] by refluxing in xylene with a trace of $NaHCO_3$, deprotection of the alcohol,[9]

* To whom correspondence should be addressed at MIT.

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