until sufficient methanol has been added to regenerate the neutral indole,[6] and under these conditions the formation of dianion, which would lead to indoline, is precluded.

Treatment of 6-methoxyquinoline (VI) in ammonia and methanol (conditions as described above) with 5 equiv of lithium afforded 32% of 5,8-dihydro-6-methoxyquinoline [IXa, bp 141–143° (8 mm); λ_{max} 6.0 μ (C=$COCH_3$), 269 mμ (ϵ 4100); nmr: δ 8.41, 7.45, and 7.08 (three protons on pyridine ring with appropriate splitting patterns), 4.83 (triplet, J = 4 cps, vinyl), and 3.58 ppm (four-proton multiplet)], 16% of 7,8-dihydro-6-methoxyquinoline [IXb, λ_{max} 275 mμ (ϵ 5900); picrate mp 164–168°; nmr (for picrate): δ 8.35, 8.01, and 7.80 (three protons on pyridine ring with appropriate splitting patterns), 5.90 (broadened singlet, vinyl), and 3.23 and 2.63 ppm (each a two-proton triplet)], 2.5% of the known[7] 5,6,7,8-tetrahydroquinoline, 5% of 6-methoxy-1,2,3,4-tetrahydroquinoline (XII), and 8% of VI.

In the absence of methanol, VI rapidly consumed 2 equiv of lithium and formed dianion VIII. Addition of methanol then afforded as the main product isolated (35%) unsymmetrical dimer XI [mp 159–160°; λ_{max} 329 and 322 (ϵ 3680), 225 mμ (ϵ 23,400); M^+ at 320; nmr: δ 8.71 and 8.00 (doublets, J = 2 cps, two protons *meta* on pyridine ring), 7.08, 7.30, and 6.97 (three protons on benzene ring), 6.60 (broad, three protons on benzene ring), 3.85 and 3.70 (two three-proton singlets, methoxyls), 2.75 and 2.05 (two two-proton multiplets), and 4.50 ppm (doubled doublet; on addition of HCl to a dimethyl sulfoxide solution of XI this splitting pattern broadened considerably, whereas the splitting patterns of the other aliphatic protons were unchanged, indicating that this proton is next to nitrogen)]. Also isolated were IX (15%) and VI (14%). Repetition of the previous experiment with 5 equiv of lithium did not afford any XI. Instead 32% of 1,2,3,4-tetrahydro-6-methoxyquinoline (XII), 5% of IXa, and 9% of VI were obtained.

With the strongly basic dianion VIII protonation apparently occurs irreversibly on nitrogen. The resulting anion is then converted by further protonation to X or its $\Delta^{3,4}$ isomer.[8] If excess lithium is present, either of these intermediates would be reduced to XII. In the absence of excess lithium, tautomerization followed by dimerization to XI occurs.

When excess methanol is present radical anion VII must be rapidly protonated before it can go to VIII. This protonation appears to be reversible on nitrogen, but irreversible on carbon (C-5) in the benzene ring,[9] leading to IXa and (by isomerization) to IXb.

Similar results were obtained with quinoline. Thus when methanol was present the main product isolated was 5,8-dihydroquinoline [picrate mp 167–169°; nmr (for picrate): δ 5.97 (two vinyl protons) and 8.75, 8.41, and 7.88 ppm (three pyridine-ring protons); 24%]. However, when the methanol was added later (5 equiv of lithium) the main product was 1,2,3,4-tetrahydroquinoline (36%).[10]

(6) This idea was originally advanced by S. O'Brien and D. C. C. Smith [*J. Chem. Soc.*, 4609 (1960)] to explain the superiority of methanol as a proton source in the reduction of indole.

(7) E. Godar and R. Mariella, *J. Am. Chem. Soc.*, **79**, 1402 (1957).

(8) When IXa was treated with lithium amide it was converted back to VI (85%) and underwent no isomerization to X.

(9) Reversal of protonation on nitrogen would be catalyzed by the methoxide formed. When ammonium chloride is substituted for the methanol no IX is formed, although reduction is nearly complete.

(10) Treatment of quinoline with 2 equiv of sodium followed by ammonium chloride (−65° under N_2) afforded 1,2-dihydroquinoline (84%) [W. Hückel and L. Hagedorn, *Chem. Ber.*, **90**, 752 (1957)].

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Pretazettine[1]

Sir:

Tazettine is considered one of the most common alkaloids of the Amaryllidaceae.[2,3] Structural studies began in 1934[4] and culminated in the assignment of structure I to the alkaloid in 1966.[5] We present evidence that tazettine is not a naturally occurring alkaloid but rather is an artifact derived from the chemical lability of the true alkaloid, pretazettine.

Because of our continuing need for large quantities of tazettine in biosynthetic studies, we selected two standard sources (*Sprekelia formosissima*[6] and *Ismene calithina*[7]) for large-scale isolation of the alkaloid. Using procedures which did not involve chromatography on alumina or any strongly basic conditions, we found the crude alkaloid fraction devoid of tazettine as determined by thin-layer chromatographic criteria.

The major alkaloid, pretazettine ($C_{18}H_{21}NO_5$), is an amorphous substance, $[\alpha]^{24}D$ +180° (*c* 0.2, $CHCl_3$). It affords crystalline hydrochloride [mp 224–225°; $[\alpha]^{24}D$ +30.3° (*c* 0.15, H_2O)] and hydrobromide [mp 224–226°; $[\alpha]^{24}D$ +19.4° (*c* 0.16, H_2O)] salts.[8] Pretazettine is readily converted to tazettine either by chromatography on basic alumina or by treatment with 0.1 *N* sodium hydroxide at 20° for 1 hr. Pretazettine is unstable as the free base and gradually rearranges to tazettine upon standing. An aqueous solution of pretazettine at 70° is converted to tazettine in less than 1 hr.

The chemical and physical properties of pretazettine are in good agreement with those reported by Proskurnina[9] for isotazettine.[10] Pretazettine may be assigned structure II not only from its ready rearrange-

(1) Supported by a grant from the National Institutes of Health (HE 7503).

(2) W. C. Wildman, *Alkaloids*, **6**, 372 (1960).

(3) H.-G. Boit, "Ergebnisse der Alkaloid-Chemie bis 1960," Akademie-Verlag, Berlin, p 410.

(4) E. Späth and L. Kahovec, *Ber.*, **67**, 1501 (1934).

(5) R. J. Highet and P. F. Highet, *Tetrahedron Letters*, 4099 (1966). Other references on the structure of tazettine include: W. I. Taylor, S. Uyeo, and H. Yajima, *J. Chem. Soc.*, 2962 (1955); T. Ikeda, W. I. Taylor, Y. Tsuda, S. Uyeo, and H. Yajima, *ibid.*, 4749 (1956); T. Ikeda, W. I. Taylor, Y. Tsuda, and S. Uyeo, *Chem. Ind.* (London), 1088 (1955); T. Ikeda, W. I. Taylor, Y. Tsuda, and S. Uyeo, *ibid.*, 411 (1956); R. J. Highet and W. C. Wildman, *ibid.*, 1159 (1955); H. Irie, Y. Tsuda, and S. Uyeo, *J. Chem. Soc.*, 1446 (1959); Y. Tsuda and S. Uyeo, *ibid.*, 2485 (1961).

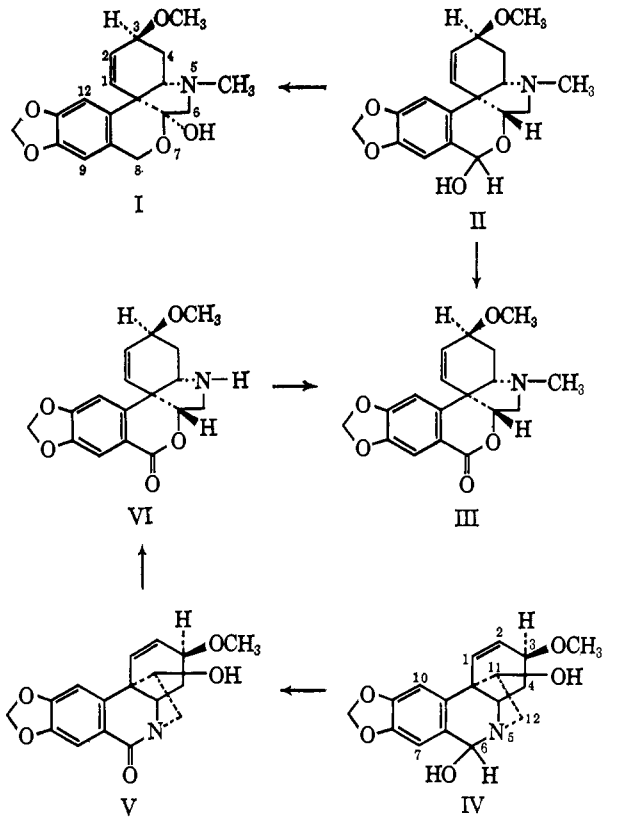
(6) H.-G. Boit and H. Ehmke, *Chem. Ber.*, **88**, 1590 (1955).

(7) H.-G. Boit and W. Döpke, *Naturwissenschaften*, **45**, 315 (1958).

(8) Substantiating elemental analyses, nmr, and mass spectral data have been obtained for all compounds and will be reported in the final paper.

(9) N. F. Proskurnina, *Zh. Obshch. Khim.*, **23**, 3365 (1957).

(10) The name isotazettine is inappropriate since it does not reflect the basic ring system of the alkaloid and introduces confusion when equated with isotazettine (criwelline), tazettinol, and isotazettinol, all of which contain the tazettine ring system but vary in stereochemistry at C_3.



ment to tazettine but also by its oxidation to III with manganese dioxide. Compound III was synthesized from haemanthidine (IV) by manganese dioxide oxidation[11] to oxohaemanthidine (V) and rearrangement to VI, mp 133–134°, $[\alpha]^{24}D$ +207° (*c* 0.36, $CHCl_3$), in aqueous acetic acid and sodium acetate. N-Methylation of VI with formaldehyde and sodium borohydride provided III, mp 127–128°, $[\alpha]^{24}D$ +276° (*c* 0.95, $CHCl_3$), identical in all respects with the manganese dioxide oxidation product of pretazettine.[12]

(11) S. Uyeo, H. M. Fales, R. J. Highet, and W. C. Wildman, *J. Am. Chem. Soc.*, 80, 2590 (1958).

(12) Preliminary research on the conversion of IV to III was carried out by Professor S. Uyeo at the National Heart Institute in 1958. The facile lactam–lactone rearrangement appears to relieve the considerable internal strain of V.

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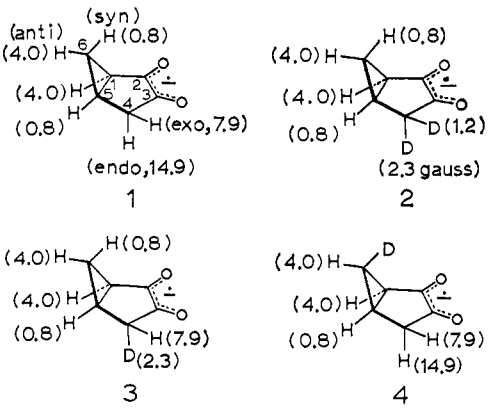
Application of Electron Spin Resonance Spectroscopy to Problems of Structure and Conformation. XI. Bicyclo[3.1.0]hexane Semidiones[1]

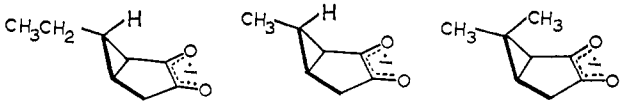
Sir:

Oxidation of a 2- or 3-oxobicyclo[3.1.0]hexane in basic dimethyl sulfoxide (DMSO) solution yields a semidione showing hyperfine splitting by six hydrogen atoms (**1**).[2] In DMSO-d_6, the 3-ketone gave semidione **2** while the 2-ketone yielded semidione **3**. Semidione **2** must result from hydrogen–deuterium exchange prior to oxidation. The stereoselective hydrogen–deuterium exchange observed in **3** occurs after oxidation and may be a property of the very weakly acidic radical anion. Stereoselective hydrogen–deuterium exchange was not found in either of the monoketones under the reaction conditions. The second methylene hydrogen in **3** will exchange in 8 hr at 25° under our reaction conditions. The 6,6-dimethyl derivative exchanges only the *endo*-hydrogen atom, even after 18 hr at 25°. The 1,5-dialkyl and the *anti*-6-alkyl derivatives also exchange the *exo*-methylene hydrogen atom at a lower rate than the unsubstituted compound. No exchange at the bridgehead positions was detected.



The 1-isopropyl-4-methylbicyclo[3.1.0]hexane-2,3-semidiones derived from β-dihydroumbellulone (*exo*-methyl) and thujone (*endo*-methyl) isomerize slowly in DMSO containing potassium *t*-butoxide to give a mixture containing approximately 90% *endo*-methyl (a^H = 6.2, 4.8, 0.8, and 0.6 gauss) and 10% *exo*-methyl (a^H = 13.9, 4.9, 0.7, and 0.6 gauss) isomers.

The assignment of hfsc to the hydrogen atoms at the C-6 position is based on semidiones **4–6** derived from the corresponding 2- or 3-ketones.[3] The 4-gauss hydrogen splitting at C-6 is present in **4** and absent in **5** and **6**.



5
a^H = 14.7, 7.8, 4.2, 0.35 gauss
$a_{CH_2}{}^H$ = 0.75 gauss

6
a^H = 14.6, 7.6, 4.3, 0.9 gauss
$a_{CH_3}{}^H$ = 0.4 gauss

7
a^H = 14.6, 7.6, 5.1, 0.9 gauss
$a_{CH_3}{}^H$ = 0.45 (one) gauss

Not only do *anti* hydrogens at C-6 interact with the unpaired spin (a double V arrangement)[4–6] but hydrogen atoms attached to alkyl groups in the *anti* C-6 position (**5**, **6**, **7**) also interact *via* 2.5 V arrangements (**8**). Even larger 2.5 V (four-bond) interactions are expected and seen in the rigid semidiones derived from

(1) This work was supported by grants from the National Science Foundation (GP-6402X) and the Army Research Office (Durham) (DA-ARO-D-31-124-G867).

(2) G. A. Russell, E. R. Talaty, and R. H. Horrocks, *J. Org. Chem.*, 32, 353 (1967).

(3) The ketonic precursor to **4** was prepared from *syn*-6-deuteriobicyclo[3.1.0]hexane-3-carboxylic acid: P. G. Gassman and F. V. Zalar, *Tetrahedron Letters*, **43**, 44, 3251 (1964). The 2-ketone precursors to **5** and **6** were prepared by the ring closure of *trans*-$RCH{=}CHCH_2CH_2COCHN_2$: M. M. Fawzi and C. David Gutche, *J. Org. Chem.*, **31**, 1390 (1966).

(4) G. A. Russell and K.-Y. Chang, *J. Am. Chem. Soc.*, **87**, 4381 (1965).

(5) G. A. Russell, K.-Y. Chang, and C. W. Jefford, *ibid.*, **87**, 4383 (1965).

(6) G. A. Russell, G. Holland, K.-Y. Chang, and L. H. Zalkow, *Tetrahedron Letters*, 1955 (1967).