pressure studies, and direct boiling point[4b] measurements now make it certain that at temperatures up to 2400°K. the vaporization process primarily involves the formation of $B_2O_3(g)$ with less than 5.0% of $B_2O_2(g)$, BO(g), or gaseous elements. The absorption and emission spectra of the equilibrium gas we have found to be identical with those obtained from boric acid–methyl alcohol flames and to correspond to the "Boric Acid Fluctuation Bands" discussed by Pearse and Gaydon.[5] Thus, the green color of boron flames must be associated with an electronic transition in the $B_2O_3(g)$ molecule.

On the basis of a highly symmetrical model for $B_2O_3(g)$ in which the two borons are on opposite sides of an equilateral triangle of oxygen atoms and with estimated bond angles and distances, one may calculate free energy functions and heat content functions. These, coupled with vapor pressure data, allow evaluation of the heat of sublimation of boric oxide and the heat of formation of $B_2O_3(g)$. In addition, our data and those of Chupka, Porter, and Inghram[2] yield values of useful thermodynamic properties for gaseous boron oxides as given in Table I. These values indicate that BO(g) is considerably less stable than suggested by Searcy and Meyers[6]; they overestimated the stability of BO(g) because they did not consider $B_2O_2(g)$ as important in the high temperature reduction of MgO with B. Earlier work of Searcy[7] on the reduction of BeO with B is more reliable since $B_2O_2(g)$ is less important at the higher temperatures.

TABLE I

THERMODYNAMIC PROPERTIES OF GASEOUS BORON OXIDES[a]

Molecule	ΔHf at 0°K., kcal./mole	Dissociation energy to gaseous atoms at 0°K., kcal./mole
BO(g)	$\geq +5.3$	≤ 189.5 (8.2 ev.)[b]
$B_2O_2(g)$	-110.9 ± 7	500.5 ± 10
$B_2O_3(g)$	-214.4 ± 5	662.9 ± 6

[a] The heat of sublimation of boron at 0°K. was taken as 135.8 kcal./mole (Alan W. Searcy, private communication 1955); the heat of formation of $B_2O_3(s)$ at 0°K. as −303.8 (data from NBS Report 3456, 1954 corrected to 0°K.); and the dissociation energy of oxygen as 117.96 kcal./mole (L. Brewer, private communication, 1955). [b] Previous values for D(BO) are 9.1 e.v from a linear Birge–Sponer extrapolation with the 0–11 vibrational levels of the ground state suggested by G. Herzberg, "Spectra of Diatomic Molecules," D. Van Nostrand Co., New York, N. Y., 1950, and 7.6 ± 0.4 ev. suggested by A. G. Gaydon, "Dissociation Energies," Chapman and Hall, Ltd., London, 1953.

Our identification of the green emission and absorption bands with the $B_2O_3(g)$ molecule is confirmed by a photometric study of the variation of the intensity of the absorption of the equilibrium gases over liquid boric oxide as a function of temperature. From the slopes of log IT *vs.* $1/T$ plots we reproduce the heat of sublimation of the gaseous molecule responsible for the green bands as 78 ± 15 kcal./mole while the effusion vapor pressure data lead to a value of 77.6 kcal./mole for $B_2O_3(g)$ over the same temperature range. The fact that we can observe the bands in absorption at 1543°K. eliminates the possibility suggested by Singh[8] that these are BO(g) bands involving the $B^2\Sigma^+$ and a higher electronic state. The Boltzmann factor would allow no appreciable population in the absorbing state. In addition, other well-known BO(g) spectra should be observable in absorption if boric oxide underwent extensive decomposition on vaporization.

(5) R. W. B. Pearse and A. G. Gaydon, "The Identification of Molecular Spectra," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 60–61.

(6) A. W. Searcy and C. E. Meyers, Technical Report on Contract No. N7onr-394/12, Project No. NR-032-331, June, 1953.

(7) A. W. Searcy, University of California Radiation Lab. Report UCRL-1404 (1951).

(8) N. L. Singh, (a) *Proc. Ind. Acad. Sci.*, **29A**, 424 (1949); (b) *J. Sci. Res. Banaras Hindu Univ.*, **2**, 147 (1951–1952).

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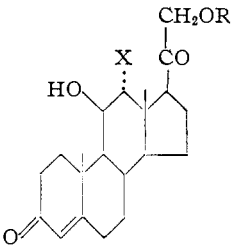
CORTICAL STEROIDS SUBSTITUTED AT C_{12}

Sir:

The introduction of halogen and other functionality at position 9 has been shown to produce important effects on the physiological properties of the parent cortical steroids as manifested in the case of the 9α-fluoro analogs by a large enhancement of both glucocorticoid and mineralocorticoid activity.[1] To date the effect of fluorine substitution at positions other than C_9 has not been reported.[2] In this communication we wish to describe a number of corticosterone and 11-dehydrocorticosterone systems substituted at position 12.



IVa, X = Br; IVb, X = Cl
IVc, X = F; IVd, X = F, Δ^1
IVe, X = F, 11 C = O;
IVf, X = OH

12α-Bromo-11-dehydrocorticosterone acetate (I)[3] was converted to its 3,20-disemicarbazone derivative, m.p. >300°; $\lambda_{max.}^{CH_3OH}$ 269 mμ (30,300), shoulder 245–250 mμ (25,200); (N, 14.8; Br, 13.7), and the latter reduced at C_{11} with lithium borohydride in tetrahydrofuran[4] followed by removal of the semicarbazone residues to give 12α-bromocorticosterone, IVa (R = H), m.p. 215–219° (dec.); $[\alpha]^{CHCl_3}D$ +126°, $\lambda_{max.}^{CH_3OH}$ 240 mμ (16,300); $\lambda_{max.}^{CHCl_3}$ 2.90, 5.87, 6.02, 6.18, μ (C, 59.75; H,

(1) (a) J. Fried and E. Sabo, THIS JOURNAL, **75**, 2273 (1953); (b) J. Fried, K. Florey, E. Sabo, J. Herz, A. Restivo, A. Borman and F. M. Singer, *ibid.*, **77**, 4181 (1955), and earlier references cited therein; (c) R. F. Hirschmann, R. Miller, R. E. Beyler, L. H. Sarett and M. Tishler, *ibid.*, **77**, 3166 (1955); (d) A. Nobile, W. Charney, P. L. Perlman, H. L. Herzog, C. C. Payne, M. E. Tully, M. A. Jevnik and E. B. Hershberg, *ibid.*, **77**, 4184 (1955); (e) J. A. Hogg, F. H. Lincoln, A. H. Nathan, A. R. Hanze, W. P. Schneider, P. F. Beal and J. Korman, *ibid.*, **77**, 4438 (1955); (f) E. Vischer, C. Meystre and A. Wettstein, *Helv. Chim. Acta*, **38**, 1502 (1955).

(2) J. E. Herz, J. Fried and E. F. Sabo have recently reported the preparation and physiological properties of 12α-halo-11β-hydroxyprogesterone, THIS JOURNAL, **78**, 2017 (1956).

(3) V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, **188**, 287 (1951).

(4) (a) Method of N. L. Wendler, Huang-Minlon and M. Tishler, THIS JOURNAL, **73**, 3818 (1951). See also (b) J. Schmidlin and A. Wettstein, *Helv. Chim. Acta*, **36**, 1241 (1953); (c) J. W. Cornforth, J. M. Osbond and G. H. Phillips, *J. Chem. Soc.*, 907 (1954).

6.59). Treatment of IVa with potassium hydroxide in methanol followed by acetylation yielded 11β,12β-oxido-Δ^4-pregnene-21-ol-3,20-dione acetate (III), m.p. 172–173°; $[\alpha]^{CHCl_3}D$ +192°; $\lambda_{max.}^{CH_3OH}$ 238.5 mμ (17,400); $\lambda_{max.}^{Nujol}$ 5.72, 5.80, 5.99, 6.17 μ (C, 71.68; H, 7.70). Reaction of the 11β,12β-oxide III with hydrogen chloride in organic solvents[4b] produced 12α-chlorocorticosterone acetate, IVb (R = CH_3CO), m.p. 228–233°; $[\alpha]^{CHCl_3}D$ +179°; $\lambda_{max.}^{CH_3OH}$ 240 mμ (15,600); $\lambda_{max.}^{Nujol}$ 2.87, 5.70, 5.80, 6.01, 6.15 μ. (C, 64.76; H, 7.27; Cl, 8.61). Similar treatment of III with hydrogen fluoride afforded 12α-fluorocorticosterone acetate, IVc (R = CH_3CO), m.p. 197–200°; $[\alpha]^{CHCl_3}D$ +209°; $\lambda_{max.}^{CH_3OH}$ 240.5 mμ (16,600); $\lambda_{max.}^{Nujol}$ 3.02, 5.70, 5.78, 6.06, 6.15 μ (C, 68.21; H, 7.67; F, 4.72). 12α-Fluoro-11-dehydrocorticosterone acetate, IVe (R = CH_3CO), m.p. 177–180°; $\lambda_{max.}^{CH_3OH}$ 237 mμ (15,800); $\lambda_{max.}^{Nujol}$ 5.75, 5.81, 5.88, 6.01, 6.20 μ; (C, 68.35; H, 7.45) was obtained from IVc (R = CH_3CO) by oxidation with sodium dichromate in acetic acid. Microbial dehydrogenation of IVc (R = CH_3CO) at positions 1:2 utilizing *Bacillus sphaericus*[5] produced 1-dehydro-12α-fluorocorticosterone, IVd (R = H) isolated, after acetylation, as its 21-acetate IVd (R = CH_3CO), m.p. 218–222°; $\lambda_{max.}^{CH_3OH}$ 242 mμ (15,700); $\lambda_{max.}^{Nujol}$ 3.08, 5.72, 5.78, 6.03, 6.18, 6.23, 11.10 μ; (C, 68.14; H, 7.11). Hydrolytic fission of the oxide III with perchloric acid[6] produced 12α-hydroxycorticosterone IVf (R = H), m.p. 208–212°; $[\alpha]^{CHCl_3}D$ +194°; $\lambda_{max.}^{CH_3OH}$ 241 mμ (15,900); $\lambda_{max.}^{Nujol}$ 2.90–3.02, 5.84, 6.08, 6.18 μ; (C, 69.97; H, 8.47) which gave, after acetylation and subsequent oxidation with chromic acid, 12α-acetoxy-11-dehydrocorticosterone acetate, II, m.p. 170–172°; $\lambda_{max.}^{CH_3OH}$ 238 (16,000); $\lambda_{max.}^{Nujol}$ 5.71, 5.80, 5.97, 6.12 μ; (C, 67.29; H, 7.06).

The 12α-fluoro analogs exhibit the same enhanced glucocorticoid activity relative to cortisone acetate as do the corresponding 9α-fluoro isomers but exhibit a somewhat lower mineralocorticoid activity than the latter.[7]

(5) T. H. Stoudt, W. J. McAleer, J. M. Chemerda, M. A. Koslowski, R. F. Hirschmann, V. Marlatt and R. Miller, *Arch. Biochem. Biophys.*, **59**, 304 (1955). We are indebted to Dr. Stoudt of these laboratories for his aid in this procedure.

(6) R. P. Graber, C. S. Snoddy, Jr., and N. L. Wendler, *Chem. & Ind.*, 57 (1956).

(7) The physiological activities were determined by Drs. C. A. Winter, C. C. Porter and H. Stoerk of the Merck Institute for Therapeutic Research and will be published in detail elsewhere.

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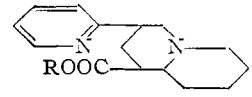
TOTAL SYNTHESIS OF OXYGENATED TETRACYCLIC LUPIN ALKALOIDS

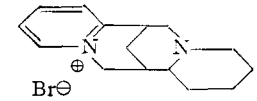
Sir:

Serving as integral units in the gradation of lupin alkaloids, the *oxygenated tetracyclic bases* (I) are flanked on the one side by cytisine and its N-alkyl derivatives (II), and on the other, by the tetracyclic oxygen-free members (III), of which sparteine is a familiar example. In recent times, members of the groups II and III have been attained through total synthesis[1]; however, the bases belonging to type (I) have been heretofore accessible only from the natural sources. Various representatives of the last class can now be produced in the laboratory, as the steps detailed below demonstrate.

Heating an aqueous alcoholic solution of 2-(α-pyridyl-allylmalonic acid[1f] and Δ^1-piperideine (as the α-trimer[2]) resulted in—as a consequence of a decarboxylative Mannich reaction accompanied by cyclization[1f]—complete assemblage of the required carbon–nitrogen skeleton, the 3-α-pyridylquinolizidine-1-carboxylic acid (IV, R = H) being isolated and purified as the ethyl ester (IV, R = C_2H_5), b.p. 155–167° (0.4 mm.) (Found: C, 70.77; H, 8.16). Subsequent to the subjection of the ester

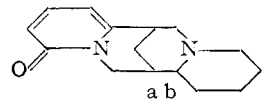


IV

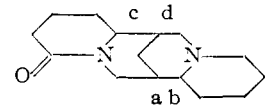


VI

to epimerization conditions (absolute ethanolic sodium ethoxide), the redistilled material was reduced with lithium aluminum hydride to the corresponding carbinol (V), b.p. 180–187° (0.3 mm.) (Found: C, 72.62; H, 8.99).[3] Conversion of V to the bromide, accomplished by means of 48% hydrobromic acid, was followed immediately by cyclization in benzene to the quaternary bromide VI, m.p. 214–216° (Found: C, 58.35; H, 7.06). Oxidation with alkaline ferricyanide led to the pyridone (VII), b.p. 170–175° (0.1 mm.), which remained a viscous oil at room temperature. The



VII



VIII

synthetic product was purified and characterized as a perchlorate (VIIa), m.p. 315°, (Found: C, 52.29; H, 6.12); and the free base, obtained from the pure salt VIIa and then distilled, exhibited a complex infrared spectrum which was identical in every detail with that of 1-*anagyrine* (VII-a,b-*trans*), the liquid[4] specimen being obtained in a comparable fashion from its pure perchlorate, m.p. 315°.[5]

The *lupanine* structure VIII (a,b-*trans*-c,d-*cis*) common (as the *d*-, *l*- or *dl*-form) to a variety of *Cytisus*, *Lupinus* and *Podalyria* genera, falls within the scope of the above synthesis, since Ing[6] has reduced anagyrine to lupanine. *Trilupine*, an alka-

(1) (a) N. J. Leonard and R. E. Beyler, THIS JOURNAL, **70**, 2299 (1948); (b) G. R. Clemo, R. Raper and W. S. Short, *Nature*, **162**, 268 (1948); (c) F. Sorm and B. Keil, *Collection Czechoslov. Chem. Commun.*, **13**, 544 (1948); (d) F. Galinovsky and G. Kainz, *Monatsh.*, **80**, 112 (1949); (e) M. Carmack, B. Douglas, E. W. Martin and H. Suss, THIS JOURNAL, **77**, 4435 (1955); (f) E. E. van Tamelen and J. S. Baran, *ibid.*, **77**, 4944 (1955); (g) F. Bohlmann, A. Englisch, N. Ottawa, H. Sander and W. Weise, *Angew. Chem.*, **67**, 708 (1955).

(2) C. Schöpf, A. Komzak, F. Braun and E. Jacobi, *Ann.*, **559**, 1 (1948).

(3) The proportions of diastereoisomers corresponding to structures IV and V were not determined.

(4) A. Partheil and L. Spasski, *Apoth. Zeit.*, **10**, 903 (1895).

(5) L. Marion and S. W. Fenton, *J. Org. Chem.*, **13**, 780 (1948).

(6) H. R. Ing, *J. Chem. Soc.*, 504 (1933).