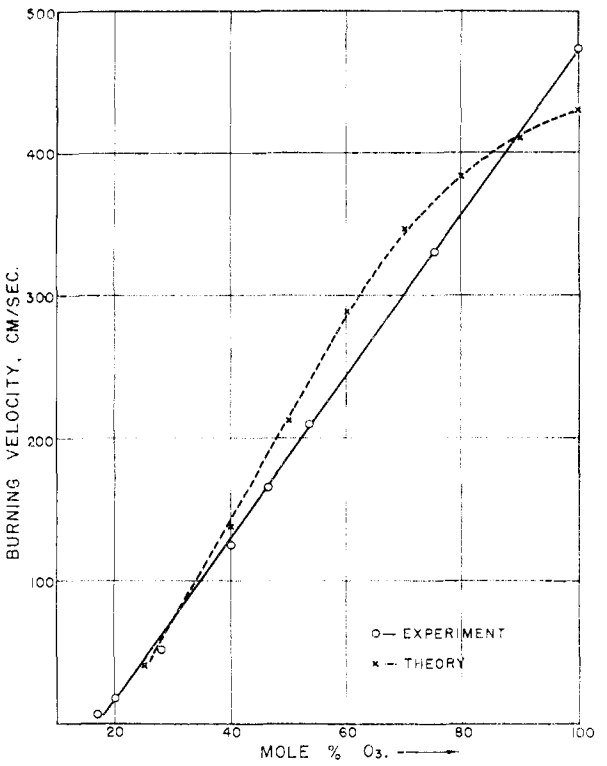

Fig. 1.—Burning velocities of ozone and ozone + oxygen mixtures (initial gas temperature = 298°K., pressure = 1 atm. abs).

pure ozone at 1 atm. pressure and at an initial temperature of 298°K. (25°C.) has a burning velocity of 472 (± 12) cm./sec.; at 195°K. it is 270 (± 7) cm./sec. Pure ozone can be burned to oxygen for substantial periods of time without explosion and detonation, like a regular combustible gas mixture.

TABLE I

1. FLAME VELOCITIES FOR INITIAL T = 298°K.

Mole % O_3	25	40	50	60	70	80	90	100
Burning velocity, V_0 (cm./s.)	41	139	214	290	349	386	411	430

Pure ozone was combusted with various fuel gases. The diffusion flame of pure ozone and cyanogen is extremely bright and produces a temperature of 5200°K. at 1.0 atm.

A detailed description of our experiments will be published elsewhere.[8]

(8) See (a) Proc. VIth International Symposium on Combustion, Aug. 19–24, 1956; (b) Proc. International Ozone Conference, Chicago, Ill., Nov. 28–30, 1956.

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A FACILE SYNTHESIS OF 2-SUBSTITUTED ADENINES[1]

Sir:

The conventional synthetic route to adenines involves the condensation of guanidine or thiourea with malononitrile to give a 4,6-diaminopyrimidine, which is then nitrosated, reduced, formylated and subsequently ring-closed.[2] The preparation of 2-alkyl- and 2-aryladenines is more cumbersome, since direct condensation of amidines with malononitrile proceeds anomalously[3] and the desired 2-substituted-4,6-diaminopyrimidines must be prepared by other methods.[4–7] The synthesis of derivatives such as isoguanine (2-hydroxy-6-aminopurine) is also circuitous, since urea does not condense satisfactorily with malononitrile and the 2-hydroxy group must be introduced indirectly.[7,8,9]

We now wish to describe a facile synthesis of 2-substituted adenines which would appear to be generally applicable. Thermal cyclization of amidine salts of isonitrosomalononitrile (I) (R = $-CH_3$; m.p. 141–142°. *Anal.* Calcd. for $C_5H_7N_5O$; C, 39.2; H, 4.6; N, 45.7. Found: C, 39.4; H, 4.4; N, 45.4. R = $-C_6H_5$; m.p. 148–150°. *Anal.* Calcd. for $C_{10}H_9N_5O$: C, 55.8; H, 4.2; N, 32.5. Found: C, 55.7; H, 4.0; N, 32.6. R = $-NH_2$; m.p. 157–158°. *Anal.* Calcd. for $C_4H_6N_6O$: C, 31.2; H, 3.9; N, 54.5. Found: C, 31.3; H, 3.9; N, 55.0) in 2-methyl-5-ethylpyridine yielded 2-substituted 4,6-diamino-5-nitrosopyrimidines (II) (R = $-CH_3$[5]; *Anal.* Found: C, 39.2; H, 4.6; N, 46.1: R = $-C_6H_5$; *Anal.* Found: C, 55.9; H, 3.9; N, 32.6: R = $-NH_2$;[10] *Anal.* Found: C, 30.7; H, 3.5; N, 55.0). The salts (I) were prepared readily in almost quantitative yield by mixing an amidine hydrochloride in ethanol solution with the silver salt of isonitrosomalononitrile,[11] removing silver chloride by filtration and concentrating the ethanol. In some instances, isolation of I was not necessary prior to cyclization; for example, heating guanidine carbonate with potassium isonitrosomalononitrile (III) (m.p. 209–211°; *Anal.* Calcd. for C_3N_3OK: N, 31.6. Found: N, 31.6) in dimethylformamide yielded 2,4,6-triamino-5-nitrosopyrimidine (II; R = $-NH_2$) in 88% yield, and condensation of III with urea in sodium ethoxide solution yielded 2-hydroxy-4,6-diamino-5-nitrosopyrimidine.[9,12]

Heating these 2-substituted 4,6-diamino-5-nitrosopyrimidines with a mixture of formamide, formic acid and sodium hydrosulfite[13] yielded 2-substituted adenines in high yield. In this manner, 2-methyladenine[5,14,15] was prepared in 74% over-

(1) This investigation was supported by a research grant (C-2551) to Princeton University from the National Cancer Institute of the National Institutes of Health, Public Health Service.

(2) For a recent review of purine chemistry, see A. Bendich in "The Nucleic Acids, Chemistry and Biology," ed. by E. Chargaff and J. N. Davidson, Vol. 1, Academic Press, New York, N. Y., 1955, p. 81.

(3) G. W. Kenner, B. Lythgoe, A. R. Todd and A. Topham, *J. Chem. Soc.*, 388 (1943).

(4) G. W. Kenner, B. Lythgoe, A. R. Todd and A. Topham, *ibid.*, 574 (1943).

(5) J. Baddiley, B. Lythgoe, D. McNeil and A. R. Todd, *ibid.*, 383 (1943).

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(7) G. A. Howard, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 476 (1944).

(8) H. L. Wheeler and G. S. Jamieson, *Am. Chem. J.*, **32**, 342 (1904).

(9) A. Bendich, J. F. Tinker and G. B. Brown, THIS JOURNAL, **70**, 3109 (1948).

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(12) H. Wieland and R. Liebig, *Ann.*, **555**, 146 (1944).

(13) H. Bredereck and A. Edenhofer, *Ber.*, **88**, 1306 (1955).

(14) H. W. Dion, D. G. Calkins and J. J. Pfiffner, THIS JOURNAL, **76**, 948 (1954).

(15) J. Baddiley, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 318 (1944).

all yield from acetamidine hydrochloride, 2-phenyladenine (*Anal.* Calcd. for $C_{11}H_9N_5$: C, 62.6; H, 4.3. Found: C, 62.7; H, 4.3) in 81% over-all yield from benzamidine hydrochloride, 2,6-diaminopurine[10,16,17] in 70% over-all yield in two steps from guanidine carbonate, and isoguanine[9] in 54% over-all yield in two steps from urea. In a preliminary experiment, 2,6-diaminopurine was prepared in 71% yield *in one step* by heating a mixture of guanidine carbonate, potassium isonitrosomalononitrile, sodium hydrosulfite and formamide for one hour. Further investigations of the potential of this strikingly simple approach to purine synthesis are in progress.

(16) L. F. Cavalieri, A. Bendich, J. F. Tinker and G. B. Brown, THIS JOURNAL, **70**, 3875 (1948).

(17) R. K. Robins, K. J. Dille, C. H. Willits and B. E. Christensen, *ibid.*, **75**, 263 (1953).

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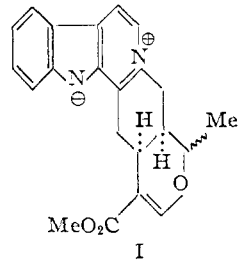
A GENERAL METHOD OF DETERMINATION OF THE STEREOCHEMISTRY OF CERTAIN INDOLE ALKALOIDS. THE STEREOCONFIGURATION OF SERPENTINE AND ALSTONINE[1]

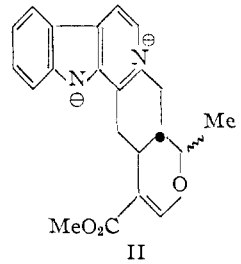
Sir:

The recently reported infrared method for determining the C-3 configuration of yohimbine- and ajmalicine-type alkaloids has permitted the ready classification of such compounds into two stereochemical categories: (1) *normal* or *allo*, and (2) *pseudo* or *epiallo* systems.[2] It is the purpose of the present communication to present a procedure for differentiating between *pseudo* and *epiallo* compounds, which, in view of the interconvertibility of (a) *normal* and *pseudo*, and (b) *allo* and *epiallo* products,[2,3,4] is also *the first general method for rapid elucidation of the relative configuration of all bridgehead hydrogen atoms, C-3, 15 and 20, of an indole alkaloid.*[5]

Palladium-maleic acid dehydrogenation of *epiallo* compounds proceeds at a rate appreciably lower than that of their *pseudo* analogs.[6] In view of the heterogeneous nature of the reaction and the irreproducibility of catalyst activity from one batch of catalyst to the next no absolute rate data were available. However semiquantitative relative rate results could be obtained by carrying out a series of simultaneous dehydrogenations on *epiallo* and *pseudo* derivatives, using the Majima method[6] under identical conditions, quenching the reactions at an arbitrary reaction time, based on a prior qualitative inspection of the catalyst activity, and undergoing an ultraviolet spectrophotometric comparison of the reaction mixtures with known standard mixtures of yohimbine and tetradehydroyohimbine. Thus (1) a four-hour run on 3-epi-α-yohimbine[7] and ψ-yohimbine[7] showed 25 and 90% oxidation, respectively, (2) an eight-hour run on 3-epi-α-yohimbyl[7] and ψ-yohimbyl alcohols [ψ-yohimbyl alcohol perchlorate, m.p. 290–291° (found: C, 56.33; H, 6.49; N, 6.46)] 65 and 90%, and (3) a four-hour run on *d,l*-epialloyohimbane[7] and ψ-yohimbane[2] 45 and 50%. Similar data on a number of combinations of *normal* or *allo* and *epiallo* derivatives also indicate the last to undergo dehydrogenation with the slowest rates. Finally, eight-hour runs on 3-isoajmalicine[2] and akuammigine,[7] showing 0 and 90% conversion, reveal them to be *epiallo* and *pseudo* products, respectively. Consequently, serpentine possesses structure I, while ajmalicine is its *allo* derivative.[8] Since the oxidation product of akuammigine, isolated as perchlorate, is identical with alstonine[7] perchlorate in infrared spectrum, melting point, 247–248° (no depression on admixture), and specific rotation $[\alpha]^{25}D + 152°$ (methanol), akuammigine can now be considered as 3-isotetrahydroalstonine, tetrahydroalstonine as having a *normal* configuration and alstonine as consisting of structure II.[9]

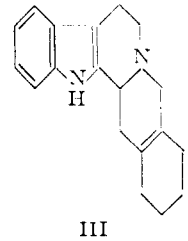


I

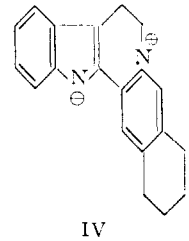


II

Catalytic ring C dehydrogenation has been found to be of general applicability and hence more useful than lead tetracetate oxidation.[7] Compounds as varied in stereochemistry and substituents as ajmalicine, yohimbone and deserpidine are transformed into serpentine, tetradehydroyohimbone [nitrate, m.p. 275–277° (found for $C_{19}H_{18}ON_2$·



III



IV

(1) This work was supported in part by a research grant (M1301) from the National Institutes of Health, Public Health Service, Department of Health, Education and Welfare.

(2) E. Wenkert and D. K. Roychaudhuri, THIS JOURNAL, **78**, 6417 (1956).

(3) F. L. Weisenborn and P. A. Diassi, *ibid.*, **78**, 2022 (1956).

(4) E. Wenkert and D. K. Roychaudhuri, *J. Org. Chem.*, **21**, 1315 (1956).

(5) The method is most useful for ring A unoxygenated ajmalicine-type alkaloids since the stereochemistry of yohimbine-type compounds can be ascertained equally well by application of the Oppenauer degradation to known yohimbone stereoisomers.[7]

(6) The Majima method of catalytic dehydrogenation [R. Majima and S. Murahashi, *Proc. Imp. Acad. (Tokyo)*, **10**, 314 (1934)] was first used as a stereochemically diagnostic tool by E. Wenkert and L. H. Liu, *Experientia*, **11**, 302 (1955), in their structure analysis of deserpidine and related alkaloids.

(7) For a recent review on the stereochemistry of indole alkaloids *cf.* J. E. Saxton, *Quart. Rev.*, **10**, 108 (1956).

(8) Recently Chatterjee suggested the same configuration and an axial 19-methyl group for ajmalicine on the basis of the reported inertness of the ring E enol ether toward 2,4-dinitrophenylhydrazine in contrast to ready hydrazone formation by tetrahydroalstonine [A. Chatterjee and S. K. Talapatra, *Science and Culture*, **20**, 568 (1955)]. However her interpretation of this difference of reactivity in terms of the presented stereoconfiguration left much to be desired.

(9) Mayumbine[7] must be a C-19 epimer of either ajmalicine or tetrahydroalstonine.