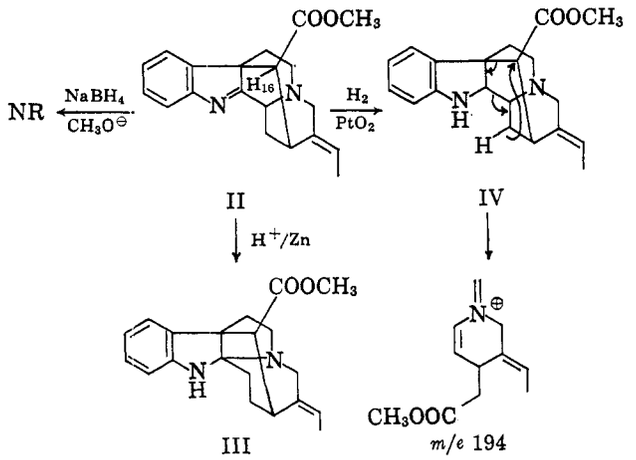
Subsequent experiments (Scheme II) bore out these assumptions and permitted assignment of structure II for strictamine. Treatment of strictamine (II) with sodium borohydride in methanol–methoxide solution left the compound unchanged, providing a strong argument against the possibility of an akuammicine[6,8,9]–aspidospermatidine[9,10] skeleton, since indolenines of this skeleton are known[8b] to undergo ring opening to the corresponding indole under such conditions. The remarkable inertness of the C=N double bond points to much greater steric hindrance around this group in II, as compared with akummicine (VII).

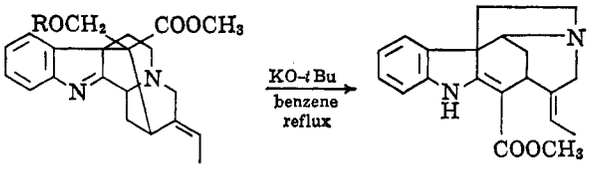
SCHEME II



Reduction of II with zinc in methanolic sulfuric acid resulted in the dihydro derivative III (mp 190–193°) which features a rearranged α-aminoindoline skeleton. The ultraviolet chromophore of this compound [λ_{max}^{EtOH} 244, 298 mμ (ϵ 7900, 3250)] suffers a hypsochromic shift in acid solution [$\lambda_{max}^{EtOH \cdot HCl}$ 235, 290 mμ (unchanged extinction)], a behavior characteristic for systems containing a Ph–N–C–N grouping.[11] Further proof that III possessed indeed a rearranged skeleton was furnished by the catalytic reduction of II to a quite different dihydroproduct, IV. The latter shows the ultraviolet bands of an indoline and its mass spectrum is quite similar to that of alcohol I [peaks at *m/e* 324 (M^+), 309 (M − 15), 251 (M − 73), 194 (166 + 28), 144, 143, 130, 122, and 121], and the interpretation of these ions is readily accommodated by the mechanism sketched above for strictaminol (I). Furthermore, reduction of IV with lithium aluminum hydride furnished the corresponding alcohol (mol wt = 296) whose mass spectrum was identical with that of I, whereas the alcohol obtained by hydride reduction of the α-aminoindoline system III showed a quite different fragmentation pattern.

It should be noted that recently the alkaloid akuammiline[12] was shown to possess structure V featuring the skeleton we propose for strictamine. Unfortunately, the published data do not permit a very meaningful comparison and correlation of our results. An important piece of evidence, cited by the French-American workers,[12] is the rearrangement (Scheme III) of deacetylakuammiline (VI) to (−)-akuammicine (VII) under treatment with strong base.

SCHEME III



V, R = Ac
VI, R = H

VII

We have been unable, as yet, to firmly duplicate this transformation with strictamine (II) itself. Reflux (1–2 hr) in benzene and potassium *t*-butoxide led to a mixture (representing about one-half of the original material) which consisted mainly of starting material and trace amounts of a compound with the same R_f value (tlc) as natural akuammicine.

It may be that equilibrium concentration of the anion derived from II by removal of the hydrogen at C-16 is very low, while during the deformylation of VI a full negative charge is developed at that position.

The representation of the stereochemistry of the carbomethoxy grouping as shown in II is based primarily upon the nmr spectrum of the compound which shows a doublet (J = 7 cps, 1 H) at 4.78 ppm which we assign to the hydrogen atom at C-16; the shielding of the indolenine nucleus would seem sufficient cause for the abnormal chemical shift.

(8) (a) K. Bernauer, W. Arnold, C. Weissman, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, **43**, 717 (1960); (b) G. F. Smith and J. T. Wrobel, *J. Chem. Soc.*, 792 (1960); (c) J. Levy, J. LeMen, and M.-M. Janot, *Bull. Soc. Chim. France*, 979 (1960).

(9) K. Biemann, "Mass Spectrometry: Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 8.

(10) K. Biemann, M. Spiteller-Friedmann, and G. Spiteller, *J. Am. Chem. Soc.*, **85**, 631 (1963).

(11) H. F. Hodson and G. F. Smith, *J. Chem. Soc.*, 1877 (1957).

(12) L. Olivier, J. Levy, J. LeMen, M.-M. Janot, H. Budzikiewicz, and C. Djerassi, *Bull. Soc. Chim. France*, 868 (1965).

The Geometry of Bisamide–Glyoxal Adducts

SIDNEY L. VAIL, ROBERT H. BARKER, AND CLIFFORD M. MORAN

Southern Regional Research Laboratory[1,2] *and Department of Chemistry, Tulane University, New Orleans, Louisiana*

Received August 31, 1965

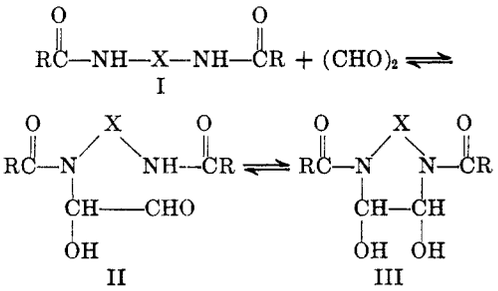
The formation of vicinal dihydroxyimidazolidines and -piperazines by the addition of alkylenebisamides (I) to glyoxal has been reported,[3] but the geometry of these adducts was not established. In a similar system, N,N′-dimethylurea was shown[4] to add nonstereospecifically to glyoxal to form equimolar amounts of *cis*- and *trans*-4,5-dihydroxy-1,3-dimethyl-2-imidazolidinone, but, under the conditions of this reaction, the less stable *cis* isomer was converted to the *trans* configuration. Rates for the formation of the *cis*- and *trans*-imidazolidones and for the conversion of the pure isomers into equilibrium mixtures at various pH values

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Inquiries should be directed to this laboratory.

(2) The mention of trade names and firms does not imply their endorsement by the Department of Agriculture over similar products or firms not mentioned.

(3) S. L. Vail, C. M. Moran, and R. H. Barker, *J. Org. Chem.*, **30**, 1195 (1965).

(4) S. L. Vail, R. H. Barker, and P. G. Mennitt, *ibid.*, **30**, 2179 (1965).



a, R = H; X = CH_2
b, R = H; X = CH_2CH_2
c, R = H; X = CH_2CHCH_3
d, R = CH_3; X = CH_2
e, R = OCH_3; X = CH_2

were examined by nmr spectroscopy. In the present work, a similar study of the bisamide–glyoxal system has been attempted.

With the exception of the unstable diformylimidazolidine (IIIa), the adducts III were subjected to periodate oxidation in order to determine their configurations. Under the conditions used, none of these heterocyclic adducts were oxidized. Similar treatment of the linear vicinal dihydroxyalkylenebisamides, N,N′-dihydroxyethylenebisacetamide, and N,N′-dihydroxyethylenebis(ethyl carbamate) gave oxidation which was essentially complete by the time the reagents were mixed. It had been previously noted[4] in the case of the dihydroxyimidazolidinones that the periodate oxidation of the *cis* isomer occurred instantaneously upon mixing while the *trans* isomer was very slow to react. Thus, the distinct lethargy of the heterocyclic bisamide adducts III toward periodate oxidation was interpreted as indicating that all of the compounds were essentially pure *trans* isomers.

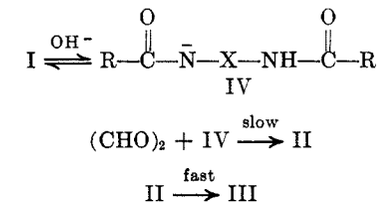
Attempts to substantiate this conclusion by nmr spectroscopy were frustrated by the unexpected complexity of the spectra of these compounds. Only compound IIIe gave a spectrum consisting solely of singlets for seemingly equivalent protons. However, this was not interpreted as indicating that the compounds were not isomerically pure since, in all but one case, the multiplets coalesced to singlets upon heating to 95° in dimethyl sulfoxide solution. The original spectra returned when the samples cooled to room temperature. Thus these multiplets would seem to be explicable in terms of restricted rotations and other slow conformational interconversions.

Because of the ambiguous nature of the nmr spectral data, it was desirable to obtain other substantiation for the assignment of *trans* configurations to the adducts. Thus a stereospecific synthesis of *trans*-1,3-diacetyl-4,5-dihydroxyimidazolidine (IIId) was carried out. Hydrogenation of imidazole over platinum oxide in excess acetic anhydride was found to produce the expected 1,3-diacetylimidazolidine[5] plus the previously unreported 1,3-diacetylimidazoline. This imidazoline was then hydroxylated with performic acid under conditions known to produce stereospecific *trans* hydroxylation.[6] The product thus obtained was found to be identical with the IIId isolated from the addition of N,N′-methylenebisacetamide to glyoxal.

(5) H. Bauer, *J. Org. Chem.*, **26**, 1649 (1961).
(6) D. Swern, *Org. Reaction*, **7**, 378.

Although nmr was of little use in the assignment of configurations, it was of use in demonstrating the effect of pH on the synthesis of the adducts III. In the N,N′-dimethylurea–glyoxal system,[4] acidic conditions produced selectively the *trans*-dihydroxyimidazolidinone whereas a mixture of isomers was formed under basic conditions. But in the alkylenebisamide additions, the products from reactions carried out under acidic and basic conditions were found to be identical. Since the N,N′-ethylenebisformamide–glyoxal addition proceeds rapidly under base catalysis, it was selected for more complete study by nmr. The reactants were mixed at a pH of 4.0, the resulting solution split into five equal parts, and each adjusted to a different pH. The reaction was followed by observing the decline and growth, respectively, of the peaks from the formyl protons of N,N′-ethylenebisformamide and the product, IIIb. The effectiveness of the base catalyst was evident. At a pH of 8.3 the reaction was 60% complete in 1 hr, while at a pH of 8.8 only 30 min was needed to reach 60% completion. It was not possible to follow the reaction beyond 60% completion since the reaction mixture became solid in the nmr sample tube at this point. In contrast to the behavior in basic solutions, the rate of addition of N,N′-ethylenebisformamide to glyoxal under acidic conditions was constant at pH values from 2.0 to 6.0. Under these conditions, *ca.* 1 week was necessary to reach 10% completion. In neither case was there evidence of significant concentrations of an intermediate, such as II, or any of the unstable *cis* isomer. These data are consistent with the mechanism shown in Scheme I. In view of previous findings (**4**), it seems

SCHEME I



unlikely that the ring closure is stereospecific. It is more probable that both *cis*- and *trans*-III are formed, but that the *cis* isomer is converted to the more stable *trans* configuration before any detectable concentration is built up.

Experimental Section[7]

Bisamide–Glyoxal Additions.—These reactions were carried out using previously described procedures.[3]

Periodate Oxidations and Titrations of III.—These titrations were carried out under the same conditions as those used previously.[4] N,N-Dihydroxyethylenebisacetamide and N,N′-dihydroxyethylenebis(ethyl carbamate) were oxidized on mixing. Essentially no oxidation of IIIb, IIIc, IIId, and IIIe was obtained. IIIa was not subjected to periodate oxidation because of the known instability of the compound. A reversal to the starting materials would produce glyoxal which is readily oxidized by periodate. In one case several grams of IIIb was dissolved in the 100 ml of periodate solution and left standing overnight.

(7) All melting points are uncorrected and were determined on a Thomas–Hoover melting point apparatus. Nmr spectra were obtained using a Varian Associates Model A-60 spectrometer. All chemical shifts are reported in parts per million downfield from tetramethylsilane as an external reference.

The sample of IIIb was recovered unchanged by chilling the solution.

1,3-Diacetyl-4-imidazoline.—Imidazole (20 g), 2 g of platinum oxide, and 400 ml of acetic anhydride were placed in a stainless steel bomb and pressurized to 500 psi with hydrogen. The bomb was rocked for 7 hr at room temperature, then opened the contents were poured over 1 kg of crushed ice. The resulting solution was evaporated *in vacuo* and the residue dissolved in ethanol. This solution was cooled and the resulting precipitate filtered. Usually, two or three crops of product were obtained with a total yield of 50%. The white, crystalline solid was recrystallized from ethanol and melted at 239–240°.

The nmr spectrum of 1,3-diacetyl-4-imidazoline in deuterium oxide at 80° consisted of singlets at 6.78, 5.48 (br), and 2.26 (sharp) ppm. The integral tracing checked very closely with the theoretical number of protons.

Anal. Calcd $C_7H_{10}N_2O_2$: C, 54.55; H, 6.49; N, 18.18. Found: C, 54.80; H, 6.50; N, 18.01.

1,3-Diacetylimidazolidine.—The third or fourth crop of crystals obtained from the ethanol solution in the synthesis of 1,3-diacetyl-4-imidazoline was a hygroscopic white solid, melting at 90–95° and identified as 1,3-diacetylimidazolidine (lit.[5] mp 95°).

Hydroxylation of 1,3-Diacetyl-4-imidazoline.—To 5.1 g of 90% formic acid was added 2.3 g of 30% hydrogen peroxide. To this solution was added slowly 1.6 g of 1,3-diacetyl-4-imidazoline. An exotherm was encountered, but the temperature of the solution was not allowed to go above 60°. After standing at room temperature for 1 hr, the solution was heated on the steam cone for 5–10 min. The solution was chilled overnight but no solids were obtained. Since the solution still contained peroxides, it was heated for 30 min on the steam cone with air blowing into the solution. On testing with potassium iodide solution, the reaction mixture was found to be almost clear of peroxides. The mixture was then evaporated to dryness under vacuum only and triturated with absolute ethanol. The solids, obtained in 30% yield, melted at 173–175° and produced an infrared spectrum identical with one from the product isolated from the addition of methylenebisacetamide to glyoxal (lit.[8] mp 176–177° for 1,3-diacetyl-4,5-dihydroxyimidazolidine).

(8) S. L. Vail, C. M. Moran, H. B. Moore, and R. M. H. Kullman, *J. Org. Chem.*, **27**, 2071 (1962).

Trialkyl Phosphates. II. Chlorination of Elemental Phosphorus in the Presence of Alcohols[1]

ARLEN W. FRANK[2] AND CHARLES F. BARANAUCKAS

Research Center, Hooker Chemical Corporation, Niagara Falls, New York 14302

Received September 24, 1965

In part I we showed that trialkyl phosphates could be prepared by the halogenation of trialkyl phosphites in the presence of alcohols.[1] Dialkyl phosphites could also be used, but they reacted more slowly. A logical development of this work was to extrapolate the synthesis back to phosphorus trihalides, and perhaps even to elemental phosphorus itself, generating the required P(III) halides and esters *in situ*. Until recently there were very few syntheses of organic phosphorus compounds in which elemental phosphorus was employed directly, but their number is growing rapidly.[3]

A reaction of phosphorus trichloride with chlorine and methanol, employing the preferred procedure[1] in which the P(III) compound and the chlorine are added simultaneously but separately to a large excess of the ice-cold alcohol, gave a 62% yield of trimethyl phosphate. This was less than the 88% yield obtained with trimethyl phosphite, but not disappointing in view of the large quantity of hydrogen chloride liberated (eq 1) and the known sensitivity of the methyl ester to acid cleavage.[1,4]

$$PCl_3 + 4ROH + Cl_2 \longrightarrow (RO)_3PO + 4HCl + RCl \quad (1)$$

Triethyl phosphate, which is less sensitive to acid cleavage, was obtained in 89% yield from phosphorus trichloride, compared to 91% from triethyl phosphite. Bliznyuk and Kolomiets[5] have since described this same reaction, obtaining an 82% yield of triethyl phosphate from phosphorus trichloride, chlorine, and ethanol at 20–25°, and have extended it to the propyl, butyl, pentyl, and octyl esters, which they obtained in 83–88% yields. The first step in our extrapolation was established.

The next step was to prepare the phosphorus trichloride *in situ* by the chlorination of elemental phosphorus in the presence of an alcohol. The formal stoichiometry of this reaction is shown in eq 2.

$$P + 2.5Cl_2 + 4ROH \longrightarrow (RO)_3PO + 4HCl + RCl \quad (2)$$

The insolubility of elemental phosphorus in alcohols posed an immediate problem. Experiments in which chlorine was passed into white phosphorus dispersed in ethanol by means of a high-speed stirrer gave a 43% yield of triethyl phosphate at −10 to 0° and a 66% yield at 25–30° (Table I).

TABLE I
CHLORINATION OF WHITE PHOSPHORUS IN ETHANOL

Reaction temp, °C	Yield of $(C_2H_5O)_3PO$, %
−10 to 0	43
25–30	66
45–50	85
78 (reflux)	46

The outcome was considerably better when the reaction was carried out at 45–50°, slightly above the melting point of white phosphorus (44.1°). The yield of triethyl phosphate was 85% (Table I), and the reaction was easier to run as it did not require a high-speed stirrer. At reflux, however, the yield of triethyl phosphate dropped to 46%.

Another problem, which caused some concern in the early stages of the investigation, was a yellow flashing which was observed when the chlorine was passed in without dilution. This phenomenon was believed to be the result of a chemiluminescent reaction between the chlorine and the phosphorus.[6] It also appeared to be the cause of a brown discoloration which sometimes made it difficult to determine the end point of the reaction. The flashing could be suppressed by diluting the chlorine with nitrogen.

(1) Part I: A. W. Frank and C. F. Baranauckas, *J. Org. Chem.*, **31**, 872 (1966).

(2) To whom correspondence should be addressed.

(3) See review by M. M. Rauhut in "Topics in Phosphorus Chemistry," Vol. 1, M. Grayson and E. J. Griffith, Ed., John Wiley and Sons, Inc., New York, N. Y., 1964, p 1.

(4) H. D. Orloff, C. J. Worrel, and F. X. Markley, *J. Am. Chem. Soc.*, **80**, 734 (1958).

(5) N. K. Bliznyuk and A. F. Kolomiets, *Zh. Obshch. Khim.*, **34**, 1169 (1964); USSR Patent 148,407 (July 13, 1962); *Chem. Abstr.*, **58**, 8906 (1963).

(6) See, for example, "Gmelins Handbuch der Anorganischen Chemie. Phosphor. Teil B," 8th ed, Verlag Chemie, Weinheim, Germany, 1964, p 283. A referee suggested that the flashing might result from an interaction of the alcohol and the chlorine alone, but we have only observed it when elemental phosphorus was present.