heating period, was evaporated to dryness *in vacuo*, water was added, and the evaporation was repeated to yield a mixture of red solid and brown tar. This was washed well with ethanol to remove the tarry material and the residue was dissolved as completely as possible in about 15 ml. of boiling butyl acetate (Darco). From the cooled filtrate 4-chloroisocarbostyril was deposited, in yields averaging 20–24%. The analytical sample was prepared by additional recrystallizations from butyl acetate, from benzene, and from acetic acid–water; white needles, m.p. 235.5–237.5° dec.

Anal. Calcd. for C_9H_6NOCl: C, 60.18; H, 3.37; N, 7.80 Found: C, 60.57; H, 3.61; N, 7.60.

The infrared spectrum showed carbonyl absorption at 1680 cm.$^{-1}$ and an additional band at 1650 cm.$^{-1}$ In addition, the usual bands ascribed to ring absorption[2] were observed at 1625 cm.$^{-1}$ and 1600 cm.$^{-1}$

When the reaction was carried out with twice as much acetic acid at steam bath temperature for 6 hr., without the second addition of peroxide, a typical yield of recrystallized product was 38%. When a reaction mixture was prepared as in the first method, but with water instead of hydrogen peroxide, and heated at 65° for 20 hr., further heating and peroxide additions by the usual procedure afforded a 40.5% yield of recrystallized product.

The chloroisocarbostyril was also prepared from a mixture of 1.45 g. of isocarbostyril, 1 ml. of 30% hydrogen peroxide, 3 ml. of glacial acetic acid, and 0.84 ml. of concentrated hydrochloric acid. On gentle warming a vigorous reaction ensued and occasional cooling was necessary for the first hour. After a final period of heating for 1 hr. at 65°, the mixture was cooled and an 87% yield of pale, orange needles, m.p. 230–236.5° dec., was separated. Recrystallization from butyl acetate (Darco) afforded white needles, m.p. 236–238° dec., in 66% yield.

Hydrolysis of 1-chloroisoquinoline. When 0.33 g. of the chloro compound was treated as in the oxidations, except that water was substituted for hydrogen peroxide, an oily solid was obtained on evaporation of most of the solvent. This was washed with warm water and with ether to leave 0.11 g. of undissolved isocarbostyril, m.p. 203–206.5°, undepressed on admixture with an authentic sample. From the filtrate a 52% yield of unchanged starting material was obtained by extraction with ether and evaporation. This had m.p. 33.5–36.5° both alone and on admixture with 1-chloroisoquinoline.

N-Acetyl-4-chloroisocarbostyril. A mixture of 1.35 g. of 4-chloroisocarbostyril and 11 ml. of acetic anhydride was refluxed for 5.5 hr., then cooled to deposit a 62% yield of long, white needles of the acetyl derivative, m.p. 105–107.5°. Evaporation of the anhydride to dryness *in vacuo* afforded an additional 36% of less pure tan solid. The analytical sample, which was recrystallized from hexane, had m.p. 105.5–107°. The compound is formulated as *N*-acetyl-4-chloroisocarbostyril, rather than as the 1-acetoxy compound, on the basis of infrared absorptions at 1723 cm.$^{-1}$ and 1685 cm.$^{-1}$ and ring absorptions at 1625 cm.$^{-1}$ and 1595 cm.$^{-1}$ A similar situation obtains with acyl derivatives of isocarbostyril.[2]

Anal. Calcd. for $C_{11}H_8NO_2Cl$: C, 59.61; H, 3.64; N, 6.32; Cl, 16.00. Found: C, 59.81; H, 3.64; N, 6.39; Cl, 15.75.

When the acetyl derivative was hydrolyzed in refluxing 10% hydrochloric acid, it was converted to 4-chloroisocarbostyril in essentially quantitative yield.

Hydrogenolysis of 4-chloroisocarbostyril. A mixture of 135 mg. of the chloro derivative, 0.1 g. of 5% palladium-on-charcoal, 0.3 g. of potassium acetate, and 20 ml. of 95% ethanol was stirred with hydrogen until slightly more than the theoretical volume had been absorbed. The catalyst was separated and the solution evaporated to dryness *in vacuo*. The isocarbostyril, after washing with water, weighed 71 mg. (65%) and had m.p. 202.5–205.5°, undepressed on admixture with the known compound.

1,4-Dichloroisoquinoline. When 0.01 mole of the chloroisocarbostyril was heated with 6 ml. of phosphorus oxychloride in a sealed tube at 120° for 4 hr., and the mixture poured

onto ice, a quantitative yield of 1,4-dichloroisoquinoline, m.p 93–94°, separated. Steam-distillation and recrystallizations from ethanol-water produced the analytical sample, long, white needles, m.p. 92–92.5° (reported[5] m.p. 88–89°).

Anal. Calcd. for $C_9H_5NCl_2$: C, 54.58; H, 2.54; N, 7.07. Found: C, 54.65; H, 2.92; N, 7.04.

The melting point was undepressed on admixture with an authentic sample prepared by the method of Gabriel.[5] A preparation more convenient than the latter involved heating a mixture of 2.90 g. of isocarbostyril and 7 g. of phosphorus pentachloride at 140° for 6 hr. The mixture was poured onto ice and the crude product recrystallized from ethanol-water; yield 50%, m.p. 92–94°.

Independent preparation of 4-chloroisocarbostyril. A solution of 1 g. of sodium and 0.6 g. of the dichloro compound in 15 ml. of methanol was heated in a sealed tube at 100° for 1.5 hr. The solvent was evaporated and the residue was washed with water to produce the crude methyl ether, m.p. 48–50°. This was not investigated further but was heated in a sealed tube with 6 ml. of concentrated hydrochloric acid at steam bath temperature for 2 hr. Addition of water allowed the separation of 4-chloroisocarbostyril, m.p. 238–238.5° dec., undepressed on admixture with material from the oxidation. The infrared spectra of the two samples were also identical. The over-all yield was 91%.

4-Bromoisocarbostyril. A mixture of 1.45 g. of isocarbostyril, 1 ml. of 30% hydrogen peroxide, and 3 ml. of glacial acetic acid was maintained at 20–25° while a solution of 1.69 g. of 48% hydrobromic acid in 1 ml. of acetic acid was added dropwise. The mixture was allowed to stand for 3 hr., then heated to 40° for 1 hr. Dilution with water afforded a 78% yield of crude 4-bromo compound, m.p. 233–237° dec. The analytical sample was recrystallized from benzene, from butyl acetate, and from 1:1 acetic acid-water; m.p. 248–249° dec.

Anal. Calcd. for C_9H_6NOBr: N, 6.25. Found: N, 6.18.

The substance was also obtained when one equivalent of potassium bromide was added to a 1-chloroisoquinoline-oxidation mixture. Initial cooling was necessary. The reaction mixture was worked up in the usual manner to produce the crude bromo compound in approximately 7% yield. After two recrystallizations the material melted at 246–248° dec.

Absorption spectra. Infrared spectra were determined with either a Perkin-Elmer or Baird spectrophotometer (KBr disk) by Dr. S. M. Nagy and associates at the Massachusetts Institute of Technology.

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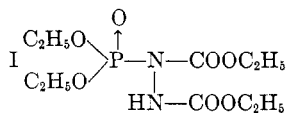## Reactions of Alkyl Phosphites with Diethyl Azodicarboxylate[1]

D. C. MORRISON

The reaction of diethyl phosphite with azodicarboxylic acid diethyl ester under alkaline catalysis was studied in the hope that the phosphite would add to the double bond of the azo group, forming a phosphoric hydrazide compound. This appeared to take place and a product was isolated which gave
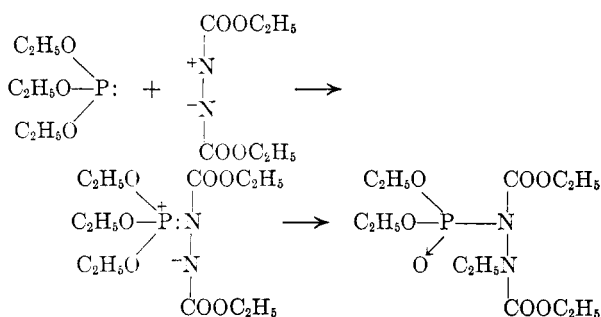
analytical values for a 1:1 adduct. It may be named diethyl phosphoric acid 1,2-dicarbethoxy hydrazide (I).

$$\begin{array}{c} \text{O} \\ \text{C}_2\text{H}_5\text{O} \quad \uparrow \\ \text{I} \quad \text{>P—N—COOC}_2\text{H}_5 \\ \text{C}_2\text{H}_5\text{O} \quad | \\ \text{HN—COOC}_2\text{H}_5 \end{array}$$

The preparative reaction is then analogous to the addition of other active hydrogen compounds to the azo ester double bond[2,3] and to the addition of dialkyl phosphites to the reactive double bond of substituted acrylic esters.[4,5] The product is a very viscous water-soluble oil. In ether solution, it reacted with sodium, evolving hydrogen. This is taken to be evidence for an NH bond, as would be required by the structure. Acid degradation of the compound gave phosphoric acid and ethyl hydrazodicarboxyate together with traces of hydrazine. The isolation of these products also supports the structure I.

Triethyl phosphite was also found to react readily with diethyl azodicarboxylate in ether solution. In this case, no catalyst was necessary and the reaction was extremely vigorous. The product was isolated by evaporation and distillation and was a somewhat more mobile oil than the product formed from diethyl phosphite. The nature of this substance is uncertain, but it is thought that the following is a rational explanation of the reaction. Polarization of the azo group may allow the positive nitrogen atom to react with the electron pair of the phosphite. The transition complex would then decompose by transference of an ethyl group from oxygen to nitrogen as shown:

$$\begin{array}{ccc} \text{C}_2\text{H}_5\text{O} & \text{COOC}_2\text{H}_5 & \\ \quad \backslash & +\text{N} & \\ \text{C}_2\text{H}_5\text{O—P:} \quad + & | & \longrightarrow \\ \quad / & -\text{N} & \\ \text{C}_2\text{H}_5\text{O} & | & \\ & \text{COOC}_2\text{H}_5 & \end{array}$$

$$\begin{array}{ccccc} \text{C}_2\text{H}_5\text{O} & \text{COOC}_2\text{H}_5 & & \text{C}_2\text{H}_5\text{O} & \text{COOC}_2\text{H}_5 \\ \quad \backslash + & | & & \quad \backslash & | \\ \text{C}_2\text{H}_5\text{O—P:N} & & \longrightarrow & \text{C}_2\text{H}_5\text{O—P——N} \\ \quad / & | & & / & | \\ \text{C}_2\text{H}_5\text{O} & -\text{N} & & \text{O} \quad \text{C}_2\text{H}_5\text{N} \\ & | & & & | \\ & \text{COOC}_2\text{H}_5 & & & \text{COOC}_2\text{H}_5 \end{array}$$

The change would be analogous to the Arbuzov rearrangement but would be intramolecular, without the usual loss of alkyl halide or equivalent. The postulated reaction product would be an ethyl derivative of the substance formed by the reaction of diethyl phosphite with the azo ester. Acid cleavage of the addition product gave phosphoric acid together with unknown substances. Trimethyl

(2) O. Diels, *Ber.*, **55**, 1524 (1922).
(3) O. Diels, *Ann.*, **429**, 1 (1922).
(4) A. N. Pudovik, *Zhur. Obshchei. Khim.*, **22**, 473 (1952); *Chem. Abstr.*, **47**, 2687 (1953).
(5) A. N. Pudovik, *Zhur. Obshchei. Khim.*, **22**, 1143 (1952); *Chem. Abstr.*, **47**, 4836 (1953).

phosphite formed a similar compound with the azo ester but it was not obtained analytically pure.

The reaction of triphenyl phosphite with azodicarboxylic ester occurs slowly at steam bath temperatures. The orange azo color disappears but no pure compound was isolated from the oily mixture.

Some preliminary work was done with triphenylphosphine. In ether solution, when the azo ester is added slowly to triphenyl phosphine solution, a white or yellowish-white precipitate is formed which soon becomes resinous and the orange azo color is destroyed. After the ether is decanted and the residue shaken with water, it crystallizes forming triphenylphosphine oxide in good yield. The supernatant probably contains diethyl hydrazodicarboxylate as the other reaction product. The phosphine oxide was confirmed by melting point and mixed melting point. The first formed resinous substance may be an analog of an ylide type compound.

EXPERIMENTAL

The diethyl azodicarboxylate was made by bromine oxidation of the corresponding hydrazo ester according to the directions of Kenner and Stedman.[6] Thiosulfate washing was avoided and several potassium carbonate washings were used instead.

Reaction of diethyl phosphite with ethyl azodicarboxylate. The diethyl phosphite should be freshly distilled before use as its hydrolysis products also react with the azo ester. The two esters did not react in anhydrous ether solution, even on warming. The reaction could be promoted by sodium methoxide but in this case methanol may add to the azo group, so sodium diethyl phosphite was employed instead. A solution was prepared containing 12.72 ml. (0.08 mole) of the azo ester and 10.24 ml. (0.08 mole) of diethyl phosphite in 50 ml. of anhydrous ether. To this was added dropwise, with stirring and cooling, a solution prepared by reaction of 3 ml. of diethyl phosphite with excess sodium in 20 ml. of anhydrous ether. Each drop of solution caused a vigorous reaction, with spattering and boiling of the ether. The addition was continued until the orange color of the ester was decolorized, only part of the catalyst solution being required. The mixture was left 0.5 hr. and 1 ml. of acetic acid added. The solution was now extracted with $^1/_2$ its volume of water and the aqueous phase re-extracted with ether. The combined ether solutions were dried over anhydrous potassium carbonate, the ether was removed, and the residue was pumped under vacuum in a water bath for several hours. The yield of crude ester was 21.7 g. or 87%. The product was distilled at 165–170°/1–2 mm. and then redistilled for analysis; *Anal.* Calcd. for $C_{10}H_{21}N_2PO_7$: C, 38.46; H, 6.73. Found: C, 38.24; H, 6.88. *d* 1.1412. The ester is an extremely viscous clear, colorless oil. It is completely water soluble. In anhydrous ether, the ester evolved hydrogen when treated with sodium.

Acid cleavage of the ester. A solution of the ester in a large excess of an equi-volume mixture of 9N hydrochloric acid and ethanol was left on the steam bath until it had evaporated to dryness. A white crystalline residue was formed which could be recrystallized from water. On purification, it had m.p. 130–132° which corresponds to that for ethyl hydrazodicarboxylate (lit. 130°[7]). This hydrazo ester is known to be very stable towards hydrolysis by strong

(6) G. W. Kenner and R. J. Stedman, *J. Chem. Soc.*, 2089 (1952).
(7) Th. Curtius and K. Heidenreich, *J. Prakt. Chem.*, **52** (160), 476 (1895).

acid.[7] The warm aqueous extract from the crystalline residue of hydrazo ester was heated with ammonium molybdate-nitric acid reagent and gave a voluminous yellow precipitate at once, showing the presence of phosphoric acid. The aqueous extract also gave a faint turbidity with saturated aqueous salicylaldehyde, indicating slight cleavage of the hydrazo ester to hydrazine.

Reaction of triethyl phosphite with ethyl azodicarboxylate. In the pure state these react violently so the action was moderated by dilution with anhydrous ether. A solution of 17.1 ml. (0.1 mole) of triethyl phosphite in 50 ml. of anhydrous ether was treated dropwise with 15.9 ml. (0.1 mole) of the azo ester under a reflux system. A few drops of the azo ester were added at first to start the reaction, and as soon as warming occurred, the remaining ester was added at such a rate that gentle refluxing of the ether took place. After the addition, the solution was refluxed for 0.5 hr. and then ether was distilled from the yellowish solution (an excess of the phosphite did not decolorize, even on heating). The residue was distilled at 170–190° at 10 mm. The product weighed 22.3 g. or 65.6%. The forerun contained a pink material which was somewhat difficult to separate from the product. The addition product was redistilled at 175–188°/10 mm. or 140–155°/2 mm. for analysis.

Anal: Calcd. for $C_{12}H_{25}N_2PO_7$ (1:1 adduct): C, 42.35; H, 7.35. Found, Prepn. I: C, 42.61; H, 6.65. Prepn. II: C, 42.80; H, 7.40.

The density of sample II was 1.1413. The product is a colorless oil, more mobile than the reaction product of diethyl phosphite. It forms two layers with water but is soluble in 30–40 volumes of water on stirring. On warming the saturated aqueous solution, the ester precipitates as an oil which redissolves on cooling.

Acid cleavage of the ester. An analytical sample was heated with an excess of concentrated hydrochloric acid on the steam bath for 12 hr. and left to evaporate on the bath to dryness. A water-soluble, very viscous colorless oil was formed. This gave a strong phosphate test with the molybdate reagent but no hydrazo ester or other crystalline material could be isolated. Only a faint turbidity was produced with salicylaldehyde.

The ester also appears to be hydrolyzed by heating for several days with dilute aqueous ammonium hydroxide. Evaporation left a viscous water-soluble sirup from which no crystalline product could be obtained.

The reaction of trimethyl phosphite with the azo ester gave a similar, distillable compound, also accompanied by a pink by-product. Analysis of the purified product for carbon gave values which were slightly higher than the theoretical.

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Isolation of *N*-Methylcytisine from *Ormosia stipitata* Schery

H. A. LLOYD AND E. C. HORNING

During the course of a study of the alkaloids of *Ormosia* species, a number of new alkaloids were isolated. Three oxygen-free compounds, ormosinine, ormosanine, and panamine and two minor oxygen-containing bases were found in *Ormosia panamensis.* Seeds of a number of other species (*O. avilensis, O. coccinea. O. jamaicensis, O. macrophylla, O. monosperma, O. tovarensis, O. costulata, O. fastigiata, O.*

nobilis, and *O. xanthocarpa*) were examined by means of paper chromatography of the alkaloid extracts. Three solvent systems were employed. The results indicated that all of the species contained approximately the same alkaloids in varying amounts.[1]

A recent collection of seeds of *O. stipitata* Schery from the province of Chiriqui, Panama, gave quite different data. Paper chromatographic examinations in various solvents revealed the presence of a large amount of one alkaloid with no indication of other bases. This alkaloid showed bright blue fluorescence under ultraviolet light, but none of the alkaloids present in the other species exhibited fluorescence.

An extraction of the seeds and purification of the alkaloid fraction was carried out on a larger scale by usual methods, and a 1.9% yield of crystalline material was obtained. The analytical data fitted the formula $C_{12}H_{16}ON_2$ and the melting point, optical rotation, and infrared spectrum were in agreement with those reported in the literature for *N*-methylcytisine. Further proof of identity was obtained by comparison of the melting point data for the hydrochloride, picrate, and perchlorate of the isolated material with literature values.

N-Methylcytisine was first found in nature by Power and Salway[2] in *Caulophyllum thalictroides* (Berberidaceae) and since then it has been obtained from many Papilionaceae either as the main alkaloid or with a number of others. A yield of the magnitude found here has not been experienced previously.

The presence of *N*-methylcytisine in *O. stipitata* seeds and its absence in the eleven other *Ormosiae* examined raises a doubt as to whether *O. stipitata* has been correctly assigned to the genus *Ormosia.* This question is currently under study by Dr. J. D. Dwyer of the Department of Biology, St. Louis University, and Dr. G. B. Schubert of the U. S. Department of Agriculture.

EXPERIMENTAL[3]

Paper chromatographic examination. A few seeds of *O. stipitata,* collected by Dr. W. H. Holdridge in Chiriqui, Panama, were crushed with a hammer, defatted with hexane, and extracted with methanol. The extract was evaporated and the residue was dissolved in dilute hydrochloric acid. This solution was placed on Whatman #1 paper and subjected to chromatography in four solvent systems. Each system yielded a single well-defined spot detected by its blue fluorescence under UV light or by spraying the paper with Munier-Dragendorf reagent. The R_f values are in Table I.

(1) H. A. Lloyd and E. C. Horning, *J. Am. Chem. Soc.,* **80,** 1506 (1958).

(2) F. B. Power and A. H. Salway, *J. Chem. Soc.,* **103,** 191 (1913).

(3) All melting points were taken on a Kofler stage. Analyses by J. F. Alicino, Metuchen, N. J.