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THE REACTION OF ALKYL PHOSPHITES WITH (*N*-PHENYLBENZIMIDOYL)FORMIC ACID*

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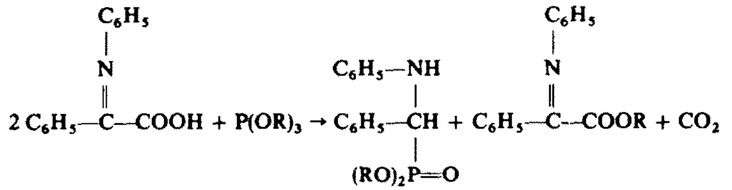
Abstract—Trimethyl and triethyl phosphites react with (*N*-phenylbenzimidoyl)formic acid (I), giving dialkyl (α-anilinobenzyl)phosphonates (II), alkyl (*N*-phenylbenzimidoyl)formates (III), CO_2 and small amounts of *N*-benzylideneaniline (IV). The effect of temperature on the reaction is studied. A mechanism for the reaction is presented which accounts for the experimental results.

At room temperature, triphenyl phosphite does not react with I; but causes its decarboxylation in boiling benzene. No reaction occurs between compound I and dialkyl phosphites.

ALTHOUGH the action of trialkyl phosphites on α-keto carboxylic acids, e.g. pyruvic acid, is known,[1] the behaviour of α-imino carboxylic acids towards the same phosphite esters has not hitherto been reported.

(*N*-Phenylbenzimidoyl)formic acid (I), for example, reacted with trimethyl phosphite at ambient temperature, in anhyd. C_6H_6, with the simultaneous evolution of CO_2. Dimethyl (α-anilinobenzyl)phosphonate (IIa) and methyl (*N*-phenylbenzimidoyl)formate (IIIa) were isolated as the main reaction products. *N*-Benzylideneaniline (IV) was also found in minor amounts. The quantity of CO_2 was determined by absorption in NaOH aq, followed by back titration with acid. The phosphonate derivative IIa was identical (comparative IR and NMR spectra) with the compound prepared by the action of dimethyl phosphite on *N*-benzylideneaniline (IV).[2] The boiling of compound IIa in C_6H_6 for 3 hr did not affect its stability. The compound decomposed, however, to *N*-benzylideneaniline and dimethyl phosphite when subjected to pyrolysis at 200°; interfering thus with its identification by gas chromatography. The identity of the Me ester IIIa was established from comparative IR spectra with an authentic sample, prepared through the action of CH_2N_2 on the acid I, and from the fact that the authentic specimen caused the exaltation of the corresponding g.c. peak of the crude



$$2\,C_6H_5\text{—}\overset{\overset{\displaystyle C_6H_5}{|}}{\underset{}{\overset{\displaystyle N}{\overset{\|}{C}}}}\text{—}COOH + P(OR)_3 \rightarrow C_6H_5\text{—}\underset{\underset{\displaystyle (RO)_2P{=}O}{|}}{\overset{\overset{\displaystyle C_6H_5\text{—}NH}{|}}{C}H} + C_6H_5\text{—}\overset{\overset{\overset{\displaystyle C_6H_5}{|}}{N}}{\overset{\|}{C}}\text{—}COOR + CO_2 \qquad 1$$

I II III

a, R = CH_3
b, R = C_2H_5

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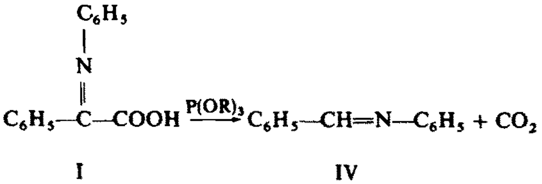
* The nomenclature of the compounds described in this paper is according to the rules of the American Chemical Society and the Chemical Abstract.

reaction mixture. The presence of IV in minute amounts among the reaction products can be tentatively explained on the premise that trimethyl phosphite—acting as a Lewis base[3]—catalyzes the decarboxylation of the acid I. In absence of trimethyl phosphite, acid I in C_6H_6, is quite stable at room temperature.



$$\underset{\text{I}}{C_6H_5{-}\overset{\overset{\displaystyle C_6H_5}{|}}{\overset{N}{\|}}{C}{-}COOH} \xrightarrow{P(OR)_3} \underset{\text{IV}}{C_6H_5{-}CH{=}N{-}C_6H_5} + CO_2 \qquad 2$$

The reaction rate and the ratio of the two main products, IIa and IIIa, were independent of the amount of trimethyl phosphite, so long that this was above 1 equiv./2 equiv. of acid I. On the basis of the amount of compound IIa formed it was concluded that reaction 1 proceeded to the extent of 90%.

When the same reaction was carried out at reflux temperature for 1 hr, the yield of *N*-benzylideneaniline increased appreciably, while that of the phosphonate adduct IIa and the methyl ester IIIa correspondingly decreased. This shows that the rate of the decarboxylation reaction is more temperature dependent than the phosphonation/esterification reaction. This is in accordance with the fact that acid I readily undergoes decarboxylation at elevated temperatures.[4]

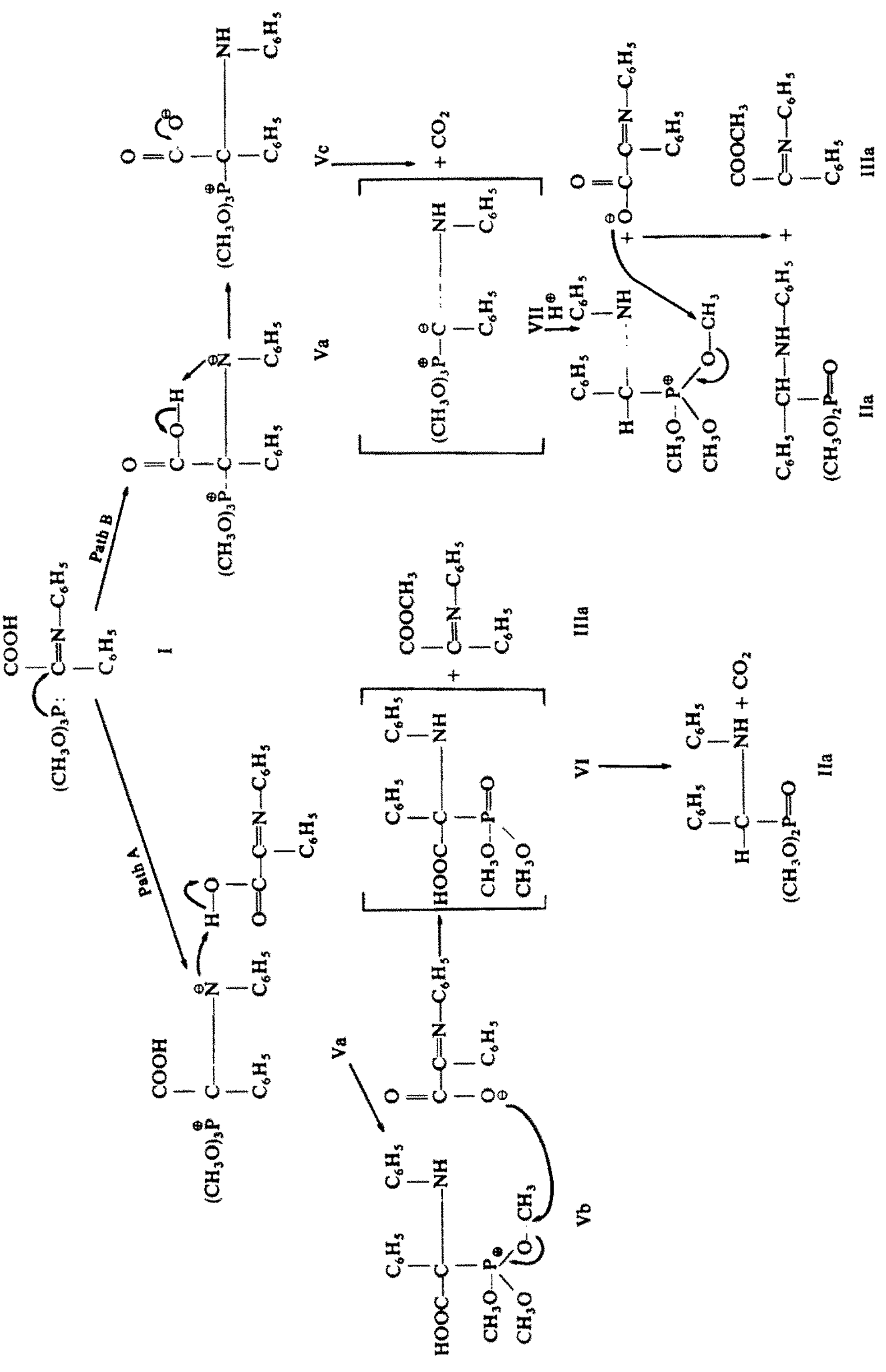
That the phosphonate adduct IIa was formed in quantities complementary to the Me ester IIIa, and that the amount of CO_2 was almost equivalent to that predicted by reaction 1, support the conclusion that these products are mechanistically related.

One can adequately explain these observations on the basis of a primary nucleophilic attack by the phosphite on the carbon atom of the azomethine group in I, giving the activated form Va. This latter, reacts with a second molecule of I, to yield IIIa and VI (Chart I, Path A). The ready decarboxylation of VI would then produce IIa together with CO_2. Supporting this idea is the fact that carboxylic acids substituted in the α-position by a phosphorus-containing group easily lose CO_2.[5] Complex Va can, however, undergo intramolecular proton rearrangement, giving the unstable ylide VII and CO_2 (Chart I, Path B). Ylide VII is assumed to extract a proton from another molecule of acid I, affording the phosphonate adduct IIa and the ester IIIa. It is difficult to distinguish between the two suggested paths. The protonation of VII could probably be followed by a temperature dependent competition between the bimolecular paths shown and the loss of trimethyl phosphite to give the *N*-benzylideneanline. This is, however, difficult to establish experimentally.

That the reaction involves a proton transfer step is supported by the finding that the Me ester of I, namely, IIIa was quite stable towards attack by trimethyl phosphite under the same experimental conditions. This stability is in variance to the behaviour of α-ketoesters, e.g. methyl pyruvate and ethyl phenylglyoxalate, towards the same reagents.[6] The reactivity of I towards trimethyl phosphite is therefore due to the proton-donating character of the molecule. Confirming this conclusion is the fact that *N*-benzylideneaniline—which is quite stable towards trimethyl phosphite—reacted readily in presence of an extra acid, e.g. AcOH, giving the phosphonate

CHART I

MECHANISM FOR THE REACTION OF TRIMETHYL PHOSPHITE WITH (*N*-PHENYLBENZIMIDOYL)FORMIC ACID



adduct IIa and MeOAc. Under these conditions the AcOH acted as a proton donor.[7]

Triethyl phosphite reacted with I in a manner analogous to that described above. On the other hand, with triphenyl phosphite at room temperature, compound I was recovered practically unchanged even after 24 hr. This behaviour is not unexpected in view of the restricted phenyl group migration in the Arbuzov reaction.[7] At reflux temperature, triphenyl phosphite caused the decarboxylation of acid I.

Due to the low nucleophilic reactivity of dialkyl phosphites $[(RO)_2P(O)H]$,[3b, 8] acid I was recovered almost unchanged after 24 hr.

EXPERIMENTAL

All m.p's are uncorrected. The trialkyl phosphites were purified by treatment with Na followed by fractional distillation and the dialkyl phosphites were freshly prepared. The C_6H_6 (thiophene-free) and the pet. ether (40–60°) were dried over Na. Alumina used for chromatography was Al_2O_3 "Woelm" neutral, activity grade II.

The IR spectra were recorded with a Carl Zeiss Infracord Spectrophotometer Model "UR 10". The gas chromatograms were carried out on a Beckman/GC-2A gas chromatograph using a silicone column (20%). NMR spectra were performed on a Varian A-60 Spectrometer.

Reaction of trimethyl phosphite with (N-*phenylbenzimidoyl*)*formic acid* (I).[4] A—*At room temperature*: The reaction vessel consisted of a 50-ml round bottom flask equipped with a thermometer, a N_2 inlet tube, a dropping funnel, and a reflux condenser. The top of the latter was connected to two gas-washing bottles containing a total of 25 ml of 0·1 N NaOH. Acid I (2·25 g, 0·01 mole) in C_6H_6 (25 ml) was placed in the reaction flask and trimethyl phosphite[9] (0·62 g, 0·005 mole) in C_6H_6 (5 ml) was introduced into the dropping funnel. N_2 was bubbled slowly into the system and the trimethyl phosphite was added dropwise, exotherm-temp. kept below 25°. After addition (*ca.* 10 min) the mixture was left at room temperature for 12 hr. Benzene was removed under reduced pressure, the oily residue (2·50 g), was treated with cold pet. ether. The solid product, obtained (1·30 g, 89·6%), m.p. 88–89° was identified as dimethyl (α-anilinobenzyl)-phosphonate (IIa) (lit.[2] m.p. 85–86°) by m.p. and comparative IR and NMR spectra, (a) $\tau = 6{\cdot}54$ and $\tau = 6{\cdot}25$ $(P(O)(OCH_3)_2$ groups, 2 doublets with $J_{H\ldots P} = 11$ cps), (b) $\tau = 5{\cdot}22$ (CH proton, d.), (c) $\tau = 3{\cdot}54 - \tau = 2{\cdot}40$ (aromatic protons, m.). The integration ratio is 6:1:10. The petroleum ether filtrate was chromatographed on Al_2O_3 (15 g). The eluate with pet. ether (0·15 g, 8·28% on the basis of reaction 2, was found identical with *N*-benzylideneaniline[10] (IV) (m. m.p.). The eluate with C_6H_6 (0·95 g, 79·5%), afforded methyl (*N*-phenylbenzimidoyl)formate (IIIa), m.p. 44–46°. (Found: C, 75·62; H, 5·62; N, 5·60; $C_{15}H_{13}NO_2$ requires: C, 75·2; H, 5·40; N, 5·80%). The ester was identical (IR) with the compound prepared by the action of CH_2N_2 on I (vide infra). Titration of the caustic solution in the wash bottles indicated the presence of 0·217 g CO_2 (92%). Repetition of the above experiment using excess trimethyl phosphite did not affect the quantities of the products.

B—*In boiling* C_6H_6: A mixture of I (2·25 g) and trimethyl phosphite (0·62 g) in C_6H_6 (30 ml) was heated under reflux for 1 hr in a reaction vessel similar to that described above. Work up yielded dimethyl (α-anilinobenzyl)phosphonate (IIa) (0·4 g, 27·5%), *N*-benzylideneaniline (1·0 g, 55·24% on the basis of reaction 2) and methyl ester IIIa (0·3 g, 25·1%). The CO_2 was determined by absorption in 0·1 N NaOH (25 ml) and found to be 0·28 g (83%). Dimethyl (α-anilinobenzyl)phosphonate (IIa) was recovered in a quantitative yield (m.p., m. m.p.), after boiling in C_6H_6 for 3 hr.

Thermal decomposition of the adduct IIa. Compound IIa (1 g) was heated (bath temperature 200°; 15 min) under reduced pressure (5 mm) in an apparatus similar to that employed for vacuum distillation (using a Liebig condenser) but without a capillary tube, the receiver being immersed in an ice–salt mixture. The reaction vessel was left to cool and small amounts of pet. ether were added. The product was recrystallized from pet. ether and proved to be *N*-benzylideneaniline (IV) (m.p., m. m.p.). The drops that formed in the receiver gave with 3,5-dinitrobenzoic acid in presence of alkali, the violet colour reaction charactaristic for dimethyl phosphite.[11]

Methyl (N-*phenylbenzimidoyl*)*formate* (IIIa). (*N*-Phenylbenzimidoyl)formic acid (I) (2·25 g) in dry ether (50 ml) was treated with an ethereal soln of CH_2N_2 (from 3 g of nitrosomethylurea).[12] The reaction vessel was kept in the ice-chest for 6 hr. After removal of ether, the residue was distilled under reduced pressure to give a yellow oil. 1·8 g, 165°/2 mm. from pentane as yellowish green crystals of IIIa. m.p. 44–46°. (Found: C, 75·31; H, 5·62; N, 5·75; $C_{15}H_{13}NO_2$ requires: C, 75·2; H, 5·40; N, 5·80%).

Adding known amounts of compound IIIa to a previously analyzed crude reaction mixture, obtained from the reaction of trimethyl phosphite with acid I, caused an increase in the corresponding g.c. peak.

Action of trimethyl phosphite on methyl (N-*phenylbenzimidoyl)formate* (IIIa). Trimethyl phosphite (1·24 g, 0·01 mole) was added to a soln of methyl (*N*-phenylbenzimidoyl)formate (2·4 g, 0·01 mole) in dry C_6H_6 (25 ml) and left at room temperature for 12 hr. After removal of the volatile materials under reduced pressure, the oily residue was triturated several times with pentane until it solidified, and crystallized from pentane to give the starting ester IIIa (m.p., m. m.p.), yield 90%. In like manner, ester IIIa was recovered unchanged, when refluxed with trimethyl phosphite in C_6H_6 for 6 hr.

Reaction of trimethyl phosphite with N-*benzylideneaniline* (IV) *in the presence of acetic acid.* In a 50-ml round bottom flask, equipped with a reflux condenser, a thermometer, and dropping funnel, were placed 18·1 g (0·1 mole) of *N*-benzylideneaniline (IV) and 6·6 g (0·11 mole) of glacial AcOH. The mixture was heated to 60°. Trimethyl phosphite (13·6 g, 0·11 mole) was added dropwise to keep temperature below 80°. After the addition of trimethyl phosphite the reaction mixture was kept at 80° for 24 hr. Distillation (atmospheric pressure) gave 5·9 g of MeOAc, identified by IR and RI (n_D^{20} 1·3593). After removal of the other volatile materials on a flash evaporator, the residue (20 g) was crystallized from pet. ether as dimethyl (α-anilinobenzyl)phosphonate (IIa), m.p. 88–89° (IR spectrum was identical with that of an authentic sample, prepared by the action of dimethyl phosphite on *N*-benzylideneaniline).[2] Repetition of the above experiment, in the absence of AcOH, yielded the *N*-benzylideneaniline, practically unchanged.

Reaction of triethyl phosphite with (N-*phenylbenzimidoyl)formic acid* (I). This was carried out in the same manner as described above. The following products were separated: (a) diethyl (α-anilinobenzyl)-phosphonate (IIb) m.p. 91° (1·25 g, 78·36%), identity established from m. m.p. and IR with an authentic sample prepared from the reaction of *N*-benzylideneaniline and diethyl phosphite.[2] (b) *N*-benzylideneaniline (0·25 g, 13·81% on the basis of reaction 2 (m.p., m. m.p.)). (c) ethyl (*N*-phenylbenzimidoyl)formate (IIIb), b.p. 180°/2 mm (0·8 g, 63·24%), proved to be identical (IR) with the compound prepared by the action of diazoethane on I (vide infra). (d) 0·22 g (90%) of CO_2.

Ethyl (N-*phenylbenzimidoyl)formate* (IIIb). To (*N*-phenylbenzimidoyl)formic acid (I) (2·2 g) was added an ethereal sln of diazoethane (from 3 g of nitrosoethylurea),[13] and the mixture was kept in the ice-chest for 12 hr. After removal of the ether, the residue was distilled under reduced pressure to give a yellow oil, 1·7 g, b.p. 180/2 mm. (Found: C, 75·60; H, 5·72; N, 5·30; $C_{16}H_{15}NO_2$ requires: C, 75·86; H, 5·96; N, 5·53%).

Attempted reaction of triphenyl phosphite with (N-*phenylbenzimidoyl)formic acid* (I). Acid I (1·1 g) in C_6H_6 (20 ml) was treated with triphenyl phosphite[14] (3 g) at room temperature for 24 hr. The acid was recovered unchanged. In boiling C_6H_6 for 3 hr, ca. 55% of the acid underwent decarboxylation to *N*-benzylideneaniline, the rest remained unchanged. Alone, acid I decomposed to the extent of 25% under similar conditions.

Action of dimethyl phosphite on I. A mixture of acid I (2·25 g, 0·01 mole) and dimethyl phosphite[15] (1·2 g, 0·011 mole) and C_6H_6 (30 ml) was left at room temperature for 24 hr. Work up in the above manner revealed the stability of the acid towards this reagent. A similar result was obtained with diethyl phosphite.

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