

Alcoholysis of Phosphorisocyanatidites

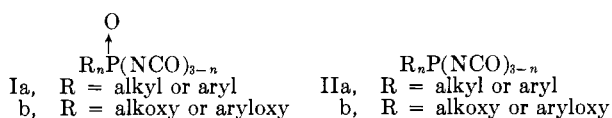
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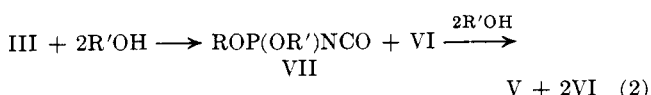
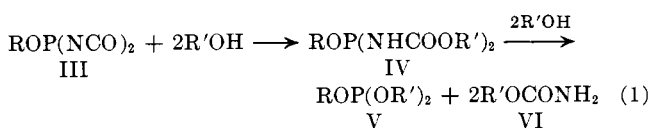
Since the first preparation of organophosphorus isocyanates by Haven¹ several other workers have reported such compounds. These were made either by reactions of the corresponding chlorides with metal cyanates^{2,3} or by a sequence of reactions starting with phosphorus pentachloride and ethyl carbamate.⁴⁻⁶ More recently, a technique using phosphorochloridites and isocyanic acid has been reported.⁷

Four classes of organophosphorus isocyanates are known: phosphonic isocyanates (Ia), phosphonous isocyanates (IIa), phosphorisocyanatidates (Ib), and phosphorisocyanatidites (IIb).



Members of the classes Ia, Ib, and IIa have been reported^{1,3,5,6} to give the expected ureas and carbamates on treatment with amines and with alcohols, respectively. A bis(benzylureide) from methyl phosphorodiisocyanatidite also has been reported recently.⁷ However, nothing was known about the reactions of phosphorisocyanatidites (IIb) with alcohols.

We have now found that class IIb compounds are readily alcoholized under very mild conditions. The alcoholysis may proceed either *via* path 1 or *via* path 2.



Using as starting materials III (R = Me or Et) and methanol or ethanol, we were unable to isolate any bis-carbamates (IV). The only products that were isolated and identified were the carbamates (VI). A gas chromatographic study of the reaction of stoichiometric amounts of III (R = Ph) with methanol at 0° showed the immediate formation of methyl carbamate (VI, R = Me) and of an unknown compound, which was tentatively identified as the half-alcoholized isocyanate (VII) (R = Ph, R' = Me). Dimethyl phenyl phosphite (V) (R = Ph, R' = Me) appeared after a few minutes. In other experiments with III (R = Me or Et) the presence of the corresponding phosphites could be detected

(1) A. C. Haven, Jr., *J. Am. Chem. Soc.*, **78**, 842 (1956).

(2) L. H. Jenkins, U. S. Patent 2,873,171 (February 10, 1959).

(3) Imperial Chemical Industries, Ltd., Belgian Patent 591,707 (November 30, 1960).

(4) A. V. Kirsanov, *Zh. Obshch. Khim.*, **24**, 1033 (1954); *Chem. Abstr.*, **49**, 8787b (1955).(5) (a) A. V. Kirsanov and I. N. Zhmurova, *Zh. Obshch. Khim.*, **26**, 2642 (1956); *Chem. Abstr.*, **51**, 1820g (1957); (b) *Zh. Obshch. Khim.*, **27**, 1002 (1957); *Chem. Abstr.*, **52**, 3715h (1958).(6) S. J. Kuhn and G. A. Olah, *Can. J. Chem.*, **40**, 1951 (1962).(7) P. R. Steyermark, *J. Org. Chem.*, **28**, 586 (1963).

by their characteristic odor nearly instantaneously on addition of a large excess of the alcohol at room temperature.

These results indicate that the direct alcoholysis of phosphorisocyanatidites, path 2, is more likely than the alcoholysis of the intermediate carbamate IV, path 1. This view also is consistent with the fact that methyl phosphorobis[(benzylcarbamoyl)amidite], CH₃OP(NHCONHCH₂Ph)₂, is stable to ethanolysis.⁷ If a bis-carbamate (IV) could be prepared, it probably also would be quite stable in an alcoholic solution.

We found that diphenyl phosphorisocyanatidate, (PhO)₂P(O)NCO, in toluene, reacts very fast with butanol at 25° under bimolecular conditions. In a solution which was 0.099 *N* with respect to both diphenyl phosphorisocyanatidate and butanol, the initial reaction rate was too high to be measured accurately; a conversion of 80%, as determined by the disappearance of the isocyanate groups, was obtained after 0.65 min., and the reaction was substantially complete in 76 min.

By comparison, a reaction of equivalent amounts of 0.114 *N* phenyl phosphorodiisocyanatidite, PhOP(NCO)₂, and butanol in toluene gave a conversion of only 3.9% in 0.90 min., 13.5% in 120 min., and 52.8% in 1240 min. The maximum conversion of 65.8% was obtained in 3340 min. The reaction obviously could not go to completion because of exhaustion of butanol due to alcoholysis of the isocyanate.

In a toluene solution in which phenyl phosphorodiisocyanatidite was 0.15 *N*, while butanol was 0.30 *N* (100% excess of butanol), disappearance of 25.7% of the isocyanate groups was measured in 0.50 min., 35.7% in 6.0 min., 60.4% in 36.0 min., 77.2% in 244.0 min., and 90.5% in 2600 min. Here the amount of butanol was sufficient for the complete alcoholysis of the isocyanate, presumably with formation of V and VI (R = Ph, R' = Bu).

The aforementioned first two examples, carried out with solutions of approximately the same normalities, suggest that the phosphorisocyanatidate is about twenty times as reactive as the phosphorisocyanatidite. Quite likely, the alcoholysis and the carbamate formation compete in both cases. While the rate of carbamate formation is considerably higher in the case of phosphorisocyanatidates, the opposite is true of phosphorisocyanatidites. Thus, the course of the reactions with alcohols depends on the kinetics of the competing reactions. The more reactive the isocyanate group, the less likely will the organophosphorus isocyanate be alcoholized.⁸

Experimental⁹

Methanolysis of Methyl Phosphorodiisocyanatidite.—A solution of 14.3 mequiv. of III (R = Me) in 10 ml. of dry tetrahydro-

(8) It has been pointed out by one of the referees that the experimental results may equally well support the reaction sequence 1, in which the first step is slow, while the second is fast. Furthermore, the second example, showing elimination of 0.658 equivalent of -NCO, indicates the presence of some phosphorus carbamate groups at the end of the reaction; otherwise, only 0.5 equivalent would be eliminated. Although we cannot exclude the possibility of the pathway 1, we feel that the disappearance of the isocyanate groups after standing several hours at room temperature may be due to reactions other than carbamate formation, e.g., dimerization and trimerization. Such reactions also would be catalyzed by butyl carbamate present in the solution.

(9) The melting points are uncorrected. Elemental analyses by Dr. C. Daessle, Montreal, Canada.

furan was added to 50 ml. of methanol. One drop of N-ethylmorpholine was added as catalyst. After 20 hr. at room temperature, the solution was concentrated at a reduced pressure, treated with petroleum ether (b.p. 30–60°) and cooled at –20°. A small amount of a crystalline powder, m.p. 180–200°, was filtered. The mother liquors were further concentrated and gave a 38% yield of methyl carbamate melting at 54–56° (acetone-petroleum ether). There was no depression of the melting point on admixture with an authentic sample.

Anal. Calcd. for $C_2H_5NO_2$: C, 32.00; H, 6.71; N, 18.66. Found: C, 32.12 and 32.23; H, 6.84 and 6.78; N, 18.82.

Ethanolysis of Ethyl Phosphorodiisocyanatidite.—A solution of 1 g. of III (R = Et) in 150 ml. of ethanol was allowed to stand at room temperature for 2 hr. It was then concentrated to a few ml. and diluted with toluene. On standing at –18° for several hours, a crystalline material melting at 49.5–51° (methanol-toluene) was obtained. The melting point was undepressed on admixture with an authentic sample of ethyl carbamate.

Anal. Calcd. for $C_2H_7NO_2$: C, 40.44; H, 7.92; N, 15.72. Found: C, 40.16; H, 8.21; N, 15.41.

In both cases the quantitative isolation of the carbamates was impossible because of their low melting points, high solubility in alcohols, and the presence of the corresponding alkyl phosphites in the crude reaction mixtures.

Kinetic Studies of the Reactions of Organophosphorus Isocyanates with Alcohols.—Solutions of the isocyanates in anhydrous solvents (toluene or tetrahydrofuran) were titrated with dibutylamine and hydrochloric acid¹⁰ to determine their normalities. Aliquots were placed in flasks protected with septums. Solutions of butanol or methanol in the same solvents were injected through the septums, while stirring magnetically, to give final solutions of known concentrations. Aliquots were withdrawn with a syringe at electrically timed intervals and added to excess dibutylamine in toluene. The excess of dibutylamine was titrated with aqueous 0.1 N HCl in the presence of bromophenol blue. Methanol or isopropyl alcohol was added to each sample before titration, to give a uniform solution without separation into layers. The initial concentration of the isocyanates was maintained at about 0.1 N, while the amount of alcohol varied from equivalent to a large excess.

Under essentially bimolecular conditions, using a 50% excess of the alcohol, the phosphorodiisocyanatidites (III, R = Me or Et) gave plots of

$$\frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)}$$

vs. time consisting of two intersecting straight lines. Under pseudo unimolecular conditions plots of $\ln a/a - x$ vs. time were rectilinear but did not pass through the origin.

Gas Chromatographic Study of the Reaction of Phenyl Phosphorodiisocyanatidite with Methanol.—A Perkin-Elmer vapor fractometer equipped with a 2-m. 5% silicon grease-Haloport F (trademark of F & M Corp., Avondale, Pa.) column was calibrated at 180° and a He pressure of 5 p.s.i.g. The following emergence times were obtained: methanol, 0.22–2.24; methyl carbamate, 0.35–0.37; dimethyl phenyl phosphite, 0.64; phenyl phosphorodiisocyanatidite, 2.20 min.

Stoichiometric amounts of III (R = Ph) and methanol were mixed at 0°. Samples, 2- μ l. each, were withdrawn from time to time and injected into the chromatographic column. An unknown peak with emergence time of 1.60–1.65 min. was observed immediately after mixing the reacting compounds. On the basis of its polarity and estimated boiling range, it was tentatively identified as VII (R = Ph, R' = Me). The experiment was continued for 205 min. During that time the following changes in the relative amounts of the components in the mixture were observed: methanol and III (R = Ph) decreased from very high to very low values, methyl carbamate and V (R = Ph, R' = Me) increased considerably, and the presumed VII (R = Ph, R' = Me) decreased from a medium to a low value.

Acknowledgment.—The author wishes to thank Professor Glen A. Russell of Iowa State University for a helpful discussion.

(10) "Spielberger's Method" reported by W. Siefken, *Ann.*, **562**, 99 (1949).

Studies on Double Acylation of Aromatic Hydrocarbons. I. Synthesis of Phenanthrene (Anthracene) by Double Succinylation of Benzene

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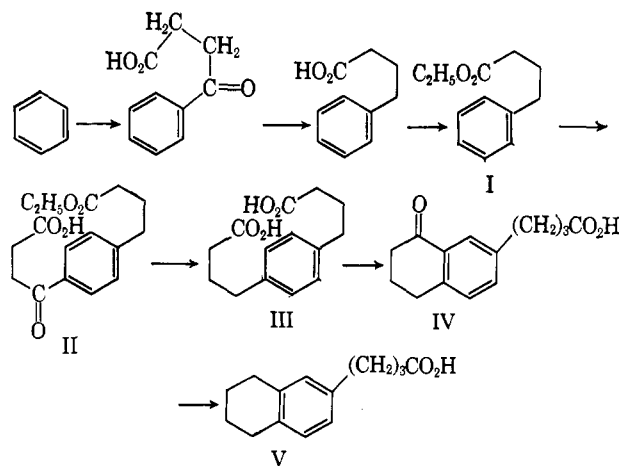
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The deactivating effect of *m*-directing substituents, such as a carbonyl group in the aromatic ring, in inter- and intramolecular acylation is well known. Thus the monosuccinoylated aromatic hydrocarbons generally cannot be subjected to further acylation. However, the reduction of the carbonyl function of the monoacylated product to a methylene group eliminates the deactivating effect of the former, and in the case of monosuccinoylated hydrocarbons separates the carbonyl group from the aromatic ring by three methylene groups, thus rendering the resulting γ -arylbutyric acid amenable to further acylation. Although the literature describes the succinylation of ethyl β -phenylpropionate¹ and phthaloylation of γ -phenylbutyric acid² as isolated examples of Friedel-Crafts acylation, no systematic work seems to have been carried out on the intermolecular acylation of aromatic hydrocarbons containing a deactivating group, e.g. a carboxyl group, removed from the aromatic ring by a few methylene entities. The present work presents results of an attempt on double succinylation of benzene.

It was considered that succinylation of a γ -arylbutyric acid obtained by the reduction of the corresponding β -arylpropionic acid, the latter containing a carbonyl group as the deactivating entity, would lead to a product which could serve as starting material for new routes to the syntheses of polynuclear hydrocarbons, through a series of steps including reduction, cyclization, and eventual dehydrogenation.

In the present work ethyl γ -phenylbutyrate³ (I) obtained by succinylation of benzene and subsequent reduction of the corresponding keto acid served as the starting material for a second succinylation of benzene.



(1) W. Borsche and F. Sinn, *Ann.*, **553**, 260 (1942).

(2) L. F. Fieser and H. Heyman, *J. Am. Chem. Soc.*, **63**, 2333 (1941).

(3) J. von Braun, *Ber.*, **44**, 2871 (1911).