TABLE I

Time at 135°,[a] hr.	6-Methoxyquinoline yield, %	6-Quinolinol yield, %	Total yield, %
8	63	2.5	65.5
10[b]	43	21	64
17	63[c]	..[d]	63
40	57	7	64
60	55	11	66
120	52	17	69
48[e]	43	12	55

[a] Maximum internal temperature, then as the reaction subsided, the bath temperature was allowed to rise to this value. [b] The boric acid was omitted. [c] Isolated by the procedure of Cromwell, Caughlin and Gilbert, THIS JOURNAL, **66**, 401 (1944). [d] Not isolated. [e] Twelve hours at a bath temperature of 155°.

until the internal temperature was 110–115°, then 25 ml. of concentrated sulfuric acid was added dropwise to the stirred reaction mixture over a period of fifteen to twenty minutes. The temperature of the reaction mixture rose gradually to 133–135° and after it started to drop, the temperature of the oil-bath was allowed to rise to 135°. After heating for forty hours, the reaction mixture was poured in 1 liter of ice and water, and the *p*-nitroanisole removed by filtration. Fifty per cent. sodium hydroxide solution was added to the filtrate until it was almost neutral then enough sodium bicarbonate was added to make the solution neutral. The mixture was extracted with benzene in a continuous extractor of the type described by Aston, *et al.*[4] This apparatus was modified by using a three-necked flask with a mechanical stirrer which speeded up the extraction process. After extraction for two days the benzene was removed by distillation, the oily residue was dissolved in 100 ml. of absolute ethanol, 12 ml. of concentrated sulfuric acid dissolved in 50 ml. of cold absolute ethanol added to precipitate the 6-methoxyquinoline as 6-methoxyquinolinium acid sulfate[5] and the mixture digested on a steam-bath for 1–1.5 hours. After cooling, the white solid was removed by filtration, washed with 25 ml. of absolute ethanol and the solid digested with 50 ml. of hot absolute ethanol, filtered and dried. The 6-methoxyquinoline was obtained from the acid sulfate by the usual procedure, as a water-clear liquid, b. p. 101–103° at 0.5 mm.; yield, 20.4 g. (57%).

The combined alcohol filtrates, after testing for complete removal of 6-methoxyquinoline by adding 1 ml. of sulfuric acid, were concentrated by distillation on a steam-bath. The residue was extracted with four 50-ml. portions of dilute ammonium hydroxide[6] (1:1), the ammoniacal solution extracted once with benzene to remove any *p*-anisidine and the aqueous portion exactly neutralized with dilute hydrochloric acid. The yield of 6-quinolinol was 2.3 g. (7%); m. p. 187–188°; recrystallized from dilute ethyl alcohol, m. p. 192–193°.[7]

Summary

6-Quinolinol as well as 6-methoxyquinoline was obtained by the Skraup reaction on *p*-methoxyacetanilide. An improved method for isolation of 6-methoxyquinoline and 6-quinolinol by a continuous extraction process has been described.

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[4] Aston, Newkirk, Jenkins, and Dorky, "Organic Syntheses," Vol. 23, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 49.

[5] Skraup, *Monatsh.*, **6**, 763 (1885), reported that the acid sulfate was insoluble in 50% ethyl alcohol but tests proved it to be slightly soluble even in 95% ethyl alcohol.

[6] The use of sodium hydroxide at the point gave mostly tars.

[7] Hargreaves, *J. Am. Pharm. Assoc.*, **25**, 975 (1936), reported a melting point of 193°.

[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

Isomerization of Alkyl Phosphites. V. The Synthesis of Phosphonoacetic and Phosphonomalonic Esters

BY GENNADY M. KOSOLAPOFF

The synthesis of triethyl phosphonoacetate has been accomplished through condensation of ethyl chloroacetate with triethyl phosphite by Arbuzov and Dunin,[1] and through the condensation of ethyl chloroacetate with sodium diethyl phosphite by P. Nylen[2] and by Arbuzov and Kamai.[3]

The latter reaction was reported by Nylen to give yields of about 50% using dry ether for the reaction solvent, while Arbuzov and Kamai reported the following effect of solvent on the yield: ligroin 56%, dry ether 59% and absolute ethanol 94.6%.

The startling improvement of the yield with the use of absolute ethanol appeared to be puzzling when the conditions under which such a reaction is run are considered. The co-presence of diethyl phosphite and sodium ethoxide may be represented by the equation

$$HPO(OC_2H_5)_2 + NaOC_2H_5 = NaPO(OC_2H_5)_2 + HOC_2H_5,$$

with a conceivable degree of equilibrium conditions, in which the proportion of sodium being linked with the phosphorus compound and with the ethanol may be varied depending on the conditions. Thus, it may be expected that the presence of an excess of ethanol would tend to push the reaction equilibrium condition considerably to the left. If this hypothesis is correct, the yields of triethyl phosphonoacetate should be lower when the reaction is run in the presence of an appreciable amount of ethanol, since in such a case the chloroacetate may tend to react to a considerable extent with the sodium ethoxide.

Accordingly, experiments were set up in which ethyl chloroacetate was treated with sodium diethyl phosphite in dry ethanol and in hexane. The results of the experiments appear to show the correctness of the above hypothesis, in that the best yield was obtained in hexane in the absence of ethanol. However, in no case could the yields

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[1] Arbuzov and Dunin, *J. Russ. Phys.-Chem. Soc.*, **46**, 295 (1914).

[2] P. Nylen, Studien über Phosphororg. Verb., Upsala, 1930.

[3] Arbuzov and Kamai, *J. Russ. Phys.-Chem. Soc.*, **61**, 619 (1929).

be made to approach the 95% figure mentioned above.

Because of the successful application of sodium dibutyl phosphite in a number of instances of syntheses of phosphonates by the writer in the past, it was thought to be possible to secure considerably better yields of phosphonoacetic ester prepared in this manner. However, the reaction of butyl chloroacetate with sodium dibutyl phosphite gave tributyl phosphonoacetate in a yield considerably lower than those previously secured with this reagent and alkyl halides, although somewhat higher than the best yield of the corresponding ethyl derivative.

The analogous possibility of preparation of phosphonomalonic esters was examined by Nylen,[2] who treated diethyl chloro- (and bromo)-malonate with sodium diethyl phosphite. Only tetraethyl ethanetetracarboxylate was reported, as an anomalous reaction product.

Because of the somewhat different mode of reaction of the trialkyl phosphites, the reaction of diethyl bromomalonate was re-examined through the use of triethyl phosphite and tributyl phosphite. Recourse was also made to sodium dibutyl phosphite. It was found that the trialkyl phosphites react readily with the bromomalonate with formation of organophosphorus derivatives, which are probably the desired phosphonomalonates. However, the thermal stability of these is rather poor, thus precluding a rigorous purification by distillation. It was interesting to note that no ethanetetracarboxylate was observed in these instances. When sodium dibutyl phosphite was used, however, Nylen's observation on the formation of the tetraethyl ethanetetracarboxylate was confirmed; at the same time there was also isolated a phosphorus-bearing ester (not mentioned by Nylen) which was probably a phosphonomalonate, but which was very poorly stable at the boiling point and could not be isolated in a satisfactory degree of purity. Hydrolysis of all of these esters led to purely organic acids, of which malonic acid was recoverable and identifiable. The bond of phosphorus to the secondary carbon was apparently quite unstable and during hydrolysis essentially complete de-phosphonation took place.

Experimental Part

Synthesis of Triethyl Phosphonoacetate

1. Twenty-three grams of sodium was dissolved in 500 cc. of absolute ethanol and the resulting solution of sodium ethoxide was treated with 138 g. of diethyl phosphite with agitation and exclusion of moisture. The solution was then treated with 123 g. of ethyl chloroacetate which was added dropwise with good agitation. The reaction was very vigorous. After the addition (three hours), the reaction mixture, which contained a large amount of sodium chloride in suspension, was allowed to stand overnight and was then centrifuged after addition of several drops of water to assist the coagulation of the precipitate. The clear centrifugate was distilled under reduced pressure to yield 52 g. (23%) of triethyl phosphonoacetate, b. p. 140–143° at 10 mm.

2. Sodium (11.5 g.) was dissolved in 400 cc. of absolute ethanol and the solution was treated with 69 g. of diethyl phosphite as in 1. Then 65 g. of ethyl chloroacetate was added dropwise to the stirred solution with efficient cooling of the mixture to substantially below room temperature. The mixture was then stirred for thirty minutes longer and allowed to stand overnight. After centrifugation as in 1, distillation of the clear solution gave 58 g. (52%) of triethyl phosphonoacetate, b. p. 140–143° at 10 mm.

3. Sodium (23 g.) was suspended with stirring in 500 cc. of hexane and was treated with 138 g. of diethyl phosphite added dropwise. When the reaction was complete, 150 g. (slight excess) of ethyl chloroacetate was added dropwise with stirring and the mixture was refluxed with stirring for three hours to ensure complete reaction of the relatively poorly soluble sodium diethyl phosphite. The mixture was worked up as above to yield 130 g. (58%) of triethyl phosphonoacetate, b. p. 140–143° at 10 mm.

Synthesis of Tributyl Phosphonoacetate.—Dibutyl phosphite (97.5 g.) reacted with 11.5 g. of sodium in 500 cc. of hexane with agitation and gentle heating. The resulting solution of sodium dibutyl phosphite was treated with 75 g. (excess) of butyl chloroacetate, which was added dropwise in the course of three hours. The mixture was heated to reflux with stirring for four hours and let stand overnight. After removal of sodium chloride by means of the centrifuge, the clear centrifugate was distilled to yield 107 g. (69%) of tributyl phosphonoacetate as a colorless liquid, b. p. 152–156° at 3 mm., $n^{25}\text{D}$ 1.4365.

Anal. Found 10.0, 10.2% P; calcd. for $C_4H_9O_2CCH_2$-$PO(OC_4H_9)_2$, 10.05% P.

Reaction of Triethyl Phosphite with Diethyl Bromomalonate.—Diethyl bromomalonate (24 g.) was placed in a round-bottomed flask equipped with a dropping funnel and a reflux condenser with a calcium chloride tube. Triethyl phosphite (16.6 g.) was added dropwise in order to moderate the otherwise very vigorous reaction over a period of one hour. The mixture was heated to 150° for four hours and distilled under reduced pressure, with evidence of appreciable instability of the product at the boiling point. There was obtained 14 g. of a yellowish liquid b. p. 153–156° at 3 mm., $n^{25}\text{D}$ 1.4358, which appeared to be substantially the tetraethyl phosphonomalonate.

Anal. Found 11.0, 11.2% P; Calcd. 10.5%. On attempted redistillation a considerable part of the material suffered further decomposition without the possibility of securing a fraction with better analytical correspondence. Hydrolysis of the product by hydrochloric acid by evaporation under an infra-red ray lamp, led to the isolation of only malonic acid in the crystalline state. The phosphorus in the hydrolyzate was substantially all inorganic.

Reaction of Tributyl Phosphite with Diethyl Bromomalonate.—Tributyl phosphite (50 g.) and diethyl bromomalonate (48 g.) were mixed in a flask equipped with a Stark–Dean trap and a reflux condenser. The mixture was heated by means of an oil-bath to 160–170° for five hours, when the reaction essentially ceased. Approximately 60% of the theoretical amount of butyl bromide was collected in the trap. After removal of the unreacted materials and low-boiling substances under reduced pressure, it was found that the residual mass was undistillable without substantial decomposition. It was a yellow somewhat viscous oil, which weighed 36 g., corresponding to 50% yield calculated as dibutyl diethyl phosphonomalonate.

Anal. Found 9.2, 9.3% P; Calcd. 8.8%. Hydrolysis by hydrochloric acid led to the same results as given above.

Reaction of Sodium Dibutyl Phosphite with Diethyl Bromomalonate.—Sodium (5.75 g.) reacted with 48.5 g. of dibutyl phosphite in 300 cc. of hexane. The solution was then treated with agitation with 60 g. of diethyl bromomalonate which was added dropwise over two hours. A fairly vigorous reaction occurred with formation of a voluminous precipitate. The mixture was stirred at room temperature for 2 hours and allowed to stand overnight. The mixture was centrifuged, the precipitate was washed with hexane on the centrifuge, and the clear combined solution was distilled under reduced pressure. The major part of the charge distilled at 130–150° at 3 mm. and crystallized on cooling. Recrystallization from alcohol gave colorless product, m. p. 76–77°, which was identified as tetraethyl ethanetetracarboxylate. Further distillation of the residue after the removal of the above fraction yielded 25 g. of a yellow oil which distilled only with very considerable decomposition at 180–200° at 3 mm. Redistillation failed to improve the product and led to further decomposition.

Anal. Found 12.6, 12.65% P; calcd. for dibutyl diethyl phosphonomalonate 8.8%. Hydrolysis by hydrochloric acid led to de-phosphonation as observed in the above examples.

Summary

It was shown that the synthesis of triethyl phosphonoacetate is favored by the use of a neutral solvent like hexane. The corresponding tributyl ester was synthesized.

The reaction of trialkyl phosphites, or to a lesser extent that of sodium dibutyl phosphite, leads to formation, with diethyl bromomalonate, of phospho-organic esters of rather poor stability, which appear to be phosphonomalonic esters.

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Vinyl Aromatic Compounds. I. The Vapor Phase Dehydration of Arylmethylcarbinols

BY DAVID T. MOWRY, MARY RENOLL[1] AND W. FREDERICK HUBER

The more common methods of preparing vinyl aromatic compounds include decarboxylation of cinnamic acids, simultaneous decarboxylation and dehydrohalogenation of β-aryl-β-halopropionic acids, dehydrogenation of ethyl aromatic compounds and dehydrohalogenation of α- or β-haloethyl aromatic compounds. A number of styrene derivatives have been prepared by the liquid phase dehydration of β-arylethyl alcohols over a basic catalyst such as potassium hydroxide[2,3] and of α-arylethyl alcohols over an acid catalyst[4–6] such as potassium bisulfate, phosphoric or oxalic acids. Of the two methods the latter is more useful because of the availability of the secondary alcohols from the reduction of the corresponding acetophenones or from the reaction of an aryl or methyl Grignard reagent with the appropriate aldehyde.

Both methods give good yields in the preparation of the more volatile vinyl aromatic compounds which do not contain substituents that are susceptible to attack by acidic or basic reagents. Unless the quantities of carbinol employed are small enough for the product to be rapidly distilled from the reaction flask, considerable loss of product through polymerization is inevitable. Furthermore, both high conversions and high yields have not often been obtained in a liquid phase reaction. To obviate these difficulties, the vapor phase dehydration[7,8] of α-phenylethyl alcohol and a few of its lower homologs has been carried out over such catalysts as alumina, thoria, or tungsten oxide at temperatures ranging from 250–500°.

After considerable experimentation with many of the above techniques, we have found that the method which most consistently gives good results for the preparation of a wide variety of vinyl aromatic compounds is the vapor phase process. Most of the twenty-three compounds listed in Table I were obtained in good yields by this method. The compounds for which ultimate analyses are given have not been previously reported.

The products were analyzed for unsaturation by the bromide–bromate method[9] and gave values ranging from 95–100% with the exception of the halogen or nitrogen substituted derivatives which gave anomalous low results by this method.

The carbinols used were prepared by reduction of the corresponding ketones. Whenever possible, hydrogenation at 120–150° using a copper chromite catalyst was employed. The by-product of this reaction was always a small amount of the analogous ethyl compound which was easily separated by distillation or crystallization. 3,4-Dichloroacetophenone and 1-chloro-4-acetylnaphthalene were reduced only with difficulty by this method, because of the tendency of the halogen compound to poison the catalyst, but were reduced smoothly with aluminum isopropoxide. Kuhn and Dann[10] obtained a 47% yield of methyl-α-thienylcarbinol together with appreciable amounts of the isopropyl ether of the product when acetothienone was reduced with aluminum isopropoxide. By using only half as much reducing agent as was employed by these authors, the yield was raised to 84% with negligible amounts of by-product ether formation. *p*-Cyanoacetophenone was also reduced with aluminum iso-

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(2) Sabatay, *Bull. soc. chim.*, **45**, 69 (1929).

(3) Sontag, *Ann. chim.*, [11] **1**, 359 (1934).

(4) Klages and Allendorff, *Ber.*, **31**, 1003, 1298 (1898).

(5) Gauthier and Gauthier, *Bull. soc. chim.*, **53**, 323 (1933).

(6) Brooks, THIS JOURNAL, **66**, 1295 (1944).

(7) French Patent 682,569 (1929), *C. A.*, **24**, 4523 (1930); German Patent 533,827 (1935).

(8) Yamamoto and Kawata, *J. Soc. Chem. Ind. Japan*, **43**, suppl. binding 279 (1940).

(9) Mulliken and Wakeman, *Ind. Eng. Chem.*, *Anal. Ed.*, **7**, 59 (1935).

(10) Kuhn and Dann, *Ann.*, **547**, 293 (1941).