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Preparation of Esters of Carboxylic and Phosphoric Acid *via* Quaternary Phosphonium Salts

Oyo MITSUNOBU*[1] and Masaaki YAMADA

Laboratory of Organic Chemistry, Tokyo Institute of Technology, Ookayama, Meguroku, Tokyo

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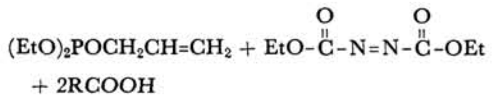
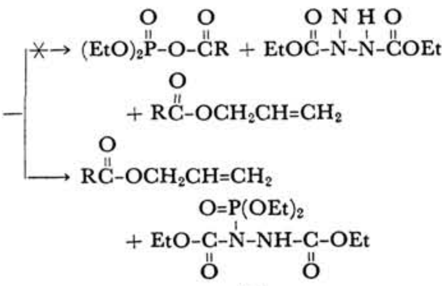
When *n*-valeric acid was treated with allyl diethyl phosphite and diethyl azodicarboxylate, allyl valeriate and diethyl *N*-(diethyl)phosphoryl hydrazodicarboxylate were obtained in good yields. Similarly ethyl benzoate was obtained in a nearly quantitative yield by the reaction of benzoic acid with triethyl phosphite and diethyl azodicarboxylate. The reaction of carboxylic acid with triphenyl phosphine and diethyl azodicarboxylate in the presence of an alcohol resulted in the formation of the corresponding esters of the carboxylic acid, triphenyl phosphine oxide, and diethyl hydrazodicarboxylate. The mechanisms of these reactions are also discussed.

The phosphorylation of alcohols by means of allyl diethyl phosphite and diethyl azodicarboxylate gave the corresponding alkyl diethyl phosphates and diethyl *N*-allyl hydrazodicarboxylate in good yields.[1]) On the other hand, when phenol was employed in place of alcohol in the above reaction, diethyl phenyl phosphate, diethyl hydrazodicarboxylate, and allyl phenyl ether were obtained.[1]) The courses of the reaction depend on the acidity of the hydroxy compounds used (alcohol; $pK_a >$ 15, phenol; $pK_a = 10$).

In this paper, in order to explore the effect of the variation in the pK_a values of hydroxy compounds, the reaction of *n*-valeric acid ($pK_a = 4.8$, 2 mol) and diethyl allyl phosphite (1 mol) with diethyl azodicarboxylate (1 mol) was first studied, on the assumption that acyl phosphate, allyl valeriate, and diethyl hydrazodicarboxylate would be formed. However, instead of the expected products, allyl valeriate and diethyl *N*-(diethyl)phosphoryl hydrazodicarboxylate (I) were obtained in 71% and 77% yields respectively, while about 1 mol of the valeric acid was recovered unchanged (54%). Similarly, the reaction of benzoic acid ($pK_a =$ 4.2) and triethyl phosphite with diethyl azodicarboxylate at room temperature resulted in the formation of ethyl benzoate and diethyl *N*-(diethyl)-phosphoryl hydrazodicarboxylate in 95% and 95% yields respectively. The results are summarized in Table 1.



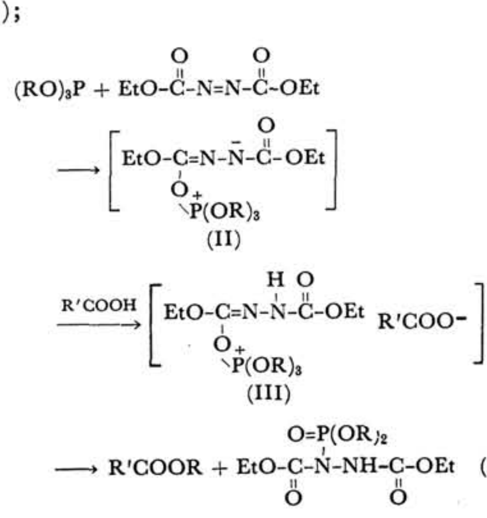
$$(EtO)_2POCH_2CH{=}CH_2 + EtO\text{-}\overset{O}{\overset{\|}{C}}\text{-}N{=}N\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt + 2RCOOH$$



$$\begin{array}{l} \not\rightarrow (EtO)_2\overset{O}{\overset{\|}{P}}\text{-}O\text{-}\overset{O}{\overset{\|}{C}}R + EtO\overset{O}{\overset{\|}{C}}\text{-}\overset{N}{\overset{|}{N}}\text{-}\overset{H}{\overset{|}{N}}\text{-}\overset{O}{\overset{\|}{C}}OEt \\ \qquad + R\overset{O}{\overset{\|}{C}}\text{-}OCH_2CH{=}CH_2 \\ \longrightarrow R\overset{O}{\overset{\|}{C}}\text{-}OCH_2CH{=}CH_2 \\ \qquad + EtO\text{-}\underset{\overset{\|}{O}}{C}\text{-}\overset{O=P(OEt)_2}{\overset{|}{N}}\text{-}NH\text{-}\underset{\overset{\|}{O}}{C}\text{-}OEt \end{array} \quad (1)$$

(I)

The reaction can be explained in the following manner. An imidoyl phosphonium salt (II) initially formed is protonated, giving an phosphonium carboxylate (III). This phosphonium carboxylate (III) is then, in turn, decomposed into an ester of carboxylic acid and diethyl *N*-(diethyl)phosphoryl hydrazodicarboxylate by the migration of the alkyl group to the carboxylate anion (Eq. (2));



$$\begin{array}{l} (RO)_3P + EtO\text{-}\overset{O}{\overset{\|}{C}}\text{-}N{=}N\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt \\ \longrightarrow \left[EtO\text{-}\underset{\underset{\underset{\searrow \overset{+}{P}(OR)_3}{O}}{|}}{C}{=}N\text{-}\overset{-}{N}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt \right] \\ \qquad\qquad (II) \\ \xrightarrow{R'COOH} \left[EtO\text{-}\underset{\underset{\underset{\searrow \overset{+}{P}(OR)_3}{O}}{|}}{C}{=}N\text{-}\overset{H}{\overset{|}{N}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt \quad R'COO^- \right] \\ \qquad\qquad (III) \\ \longrightarrow R'COOR + EtO\text{-}\underset{\overset{\|}{O}}{C}\text{-}\overset{O=P(OR)_2}{\overset{|}{N}}\text{-}NH\text{-}\underset{\overset{\|}{O}}{C}\text{-}OEt \end{array} \quad (2)$$

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[1] Present address: Department of Chemistry, College of Science and Engineering, Aoyama Gakuin University, Megurisawacho, Setagaya-ku, Tokyo.

1) O. Mitsunobu, M. Yamada and T. Mukaiyama, This Bulletin, **40**, 935 (1967).

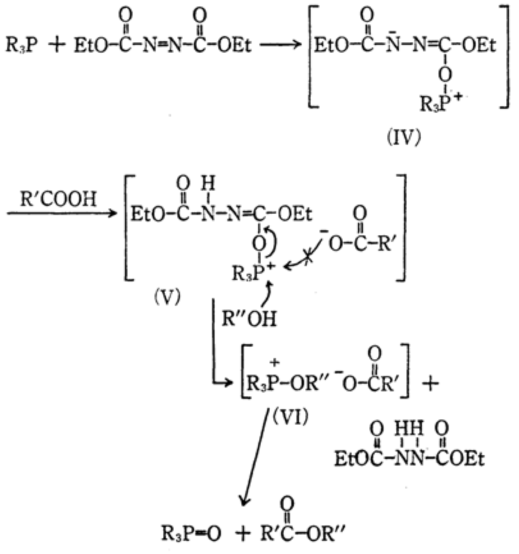
TABLE 1. ESTERIFICATION OF CARBOXYLIC ACIDS BY MEANS OF TRIALKYL PHOSPHITES AND DIETHYL AZODICARBOXYLATE

Phosphites $(EtO)_2P$-OR	Carboxylic acids R'COOH	Products							
		Esters, R'COOR							Diethyl N-(diethyl)-phosphoryl hydrazodicarboxylate
R	R'	R'	R	Yield %	Bp °C/mmHg		C	H	Yield, %
CH_2=$CHCH_2$	n-C_4H_9 (2 mol)	n-C_4H_9	CH_2CH=CH_2	71*	57—59/13	Calcd Found	67.57 67.28	9.93 9.94	77
C_2H_5	n-C_4H_9 (2 mol)	n-C_4H_9	C_2H_5	79**	73—74/53	Calcd Found	64.58 65.15	10.84 10.67	92
C_2H_5	C_6H_5	C_6H_5	C_2H_5	95	86—88/12	Calcd Found	71.88 71.82	6.71 6.61	94

* 54% of n-valeric acid was recovered based on the consumed acid.

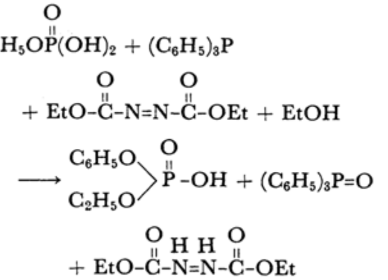
** 51% of n-valeric acid was recovered based on the consumed acid.

Next, based on the assumption described above, another attempt at the esterification of carboxylic acid was made. If the reaction of phosphine with diethyl azodicarboxylate is carried out in the presence of carboxylic acid and alcohol, a phosphonium carboxylate (V) will be formed by way of an imidoyl phosphonium salt (IV). Since the nucleophilicity of the carboxylic anion is weaker than that of alcohol, the phosphonium carboxylate (V) would be primarily attacked by the alcohol to give an alkoxy phosphonium carboxylate (VI), followed by the formation of the ester of carboxylic acid and phosphine oxide (Eq. (3));



When the reaction of benzoic acid with allyl alcohol in the presence of diethyl azodicarboxylate and triphenyl phosphine was carried out at room temperature, allyl benzoate was obtained in an 85% yield. Similarly, ethyl benzoate and isopropyl benzoate were obtained in 85% and 90% yields respectively. However, when valeric acid was used in place of benzoic acid in the above reaction, the yields of the corresponding esters were low (34—42%). The results are summarized in Table 2.

In continuing the investigation, we tried to phosphorylate an alcohol by employing the reaction mentioned above. When phenyl dihydrogen phosphate ($pK_1 = ca.\ 2$, $pK_2 = ca.\ 7$) was treated with ethanol at room temperature, ethyl phenyl hydrogen phosphate was isolated as its anilinium salt in a 45% yield (Eq. (4));



$$C_6H_5O\overset{O}{\overset{\|}{P}}(OH)_2 + (C_6H_5)_3P + EtO\text{-}\overset{O}{\overset{\|}{C}}\text{-}N{=}N\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt + EtOH \longrightarrow (C_6H_5O)(C_2H_5O)\overset{O}{\overset{\|}{P}}\text{-}OH + (C_6H_5)_3P{=}O + EtO\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{H}{N}\text{-}\overset{H}{N}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt \qquad (4)$$

It has been reported[2] that the reaction of quinone dibenzimide with tri-n-butyl phosphine in the presence of 2 mol of phosphoric monoesters resulted in the formation of the corresponding pyrophosphates in good yields. Similarly, the phosphoric diester has been produced by the reaction of quinone dibenzimide, tri-n-butyl phosphine, and phosphoric monoester with alcohol. However, an undesired side product, pyrophosphate, has also been formed.[3]

No pyrophosphate was formed, as indicated by paper chromatography, in the phosphorylation of ethanol by the present method.

Experimental

Diethyl azodicarboxylate[4] and allyl diethyl phosphite[5] were prepared by the procedures given in the literature. Triphenyl phosphine, triethyl phosphite,

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[2] I. Kuwazima and T. Mukaiyama, *J. Org. Chem.*, **29**, 1385 (1964).

[3] I. Kuwazima and T. Mukaiyama, unpublished.

[4] N. Robjohn, "Organic Syntheses," Coll. Vol. III, p. 375 (1955).

[5] A. N. Pudvik and I. M. Aladzheva, *Chem. Abstr.*, **60**, 1788 (1964).

TABLE 2. ESTERIFICATION OF CARBOXYLIC ACIDS BY MEANS OF TRIPHENYL PHOSPHINE AND DIETHYL AZODICARBOXYLATE IN THE PRESENCE OF ALCOHOLS

Carboxylic acids RCOOH	Alcohols R'OH	Product Esters, RCOOR'			
R	R'	R	R'	Yields, %	Bp, °C/mmHg
n-C_4H_9	CH_2=$CHCH_2$	n-C_4H_9	CH_2=$CHCH_2$	35	57—59/12
n-C_4H_9	C_2H_5	n-C_4H_9	C_2H_5	34	60—63/28—33
n-C_4H_9	*iso*-C_3H_7	n-C_4H_9	*iso*-C_3H_7	43	
C_6H_5	CH_2=$CHCH_2$	C_6H_5	CH_2=$CHCH_2$	85	102—105/12
C_6H_5	C_2H_5	C_6H_5	C_2H_5	85	97—100/19
C_6H_5	*iso*-C_3H_7	C_6H_5	*iso*-C_3H_7	90	103—106/17

n-valeric acid, and benzoic acid were obtained from commercial sources and were purified by recrystallization or redistillation. The solvents and alcohols were purified and dried by ordinary procedures.

Preparation of Esters of Carboxylic Acid by the Reaction of Diethyl Azodicarboxylate with Carboxylic Acid and Trialkyl Phosphite. *(A) Allyl Valeriate.* A solution of diethyl allyl phosphite (1.78 g, 0.01 mol) in 5 m*l* of ether was added, drop by drop, into a solution of diethyl azodicarboxylate (1.74 g, 0.01 mol) and *n*-valeric acid (2.04 g, 0.02 mol) in 10 m*l* of ether, under vigorous stirring at room temperature. After the solution had been kept standing overnight at room temperature, allyl valeriate (1.00 g, 70.6%, bp 57—63°C/14 mmHg; redistillation gave bp 57—59°C/13 mmHg. Found: C, 67.28; H, 9.94%) and diethyl *N*-(diethyl)phosphoryl hydrazodicarboxylate (2.40 g, 77.0%, bp 150—167°C/0.1 mmHg; redistillation gave an analytical sample, bp 160—165°C/0.18—0.20 mmHg) were obtained by fractionation. At the same time, 53.9% (1.10 g) of *n*-valeric acid (bp 77—83°C/10 mmHg) was recovered.

Found: C, 39.38; H, 6.79; N, 9.69%. Calcd for $C_{10}H_{21}N_2O_7P$: C, 38.46; H, 6.78; N, 8.97%. IR, ν (liquid) cm^{-1}: 3250 (N–H), 1740 (C=O), 1260 (P=O) 1160 (P–OEt).

(B) Ethyl Benzoate. A solution of triethyl phosphite (1.66 g, 0.01 mol) in 4 m*l* of ether was added, drop by drop, into a solution of diethyl azodicarboxylate (1.74 g, 0.01 mol) and benzoic acid (1.22 g, 0.01 mol) in 8 m*l* of ether under vigorous stirring at room temperature. The reaction soon started, with a liberation of heat. After the solution had been kept standing overnight at room temperature, ethyl benzoate (1.42 g, 94.7%, bp 86—88°C/12 mmHg. Redistillation gave an analytical sample, bp 88—90°C/11 mmHg. Found: C, 71.82; H, 6.61%) and diethyl *N*-(diethyl)phosphoryl hydrazodicarboxylate (2.95 g, 94.6%) were obtained by fractionation.

Preparation of Esters of Carboxylic Acid by the Reaction of Triphenyl Phosphine, Alcohol, and Carboxylic Acid with Diethyl Azodicarboxylate. *General Procedure.* A solution of triphenyl phosphine (0.01 mol) in 10 m*l* of ether was added drop by drop, into a solution of diethyl azodicarboxylate (0.01 mol) and carboxylic acid (0.01 mol) in 10 m*l* of ether, under vigorous stirring at room temperature. The reaction soon started, and a white precipitate of triphenyl phosphine oxide and diethyl hydrazodicarboxylate appeared. After the solution had been kept standing overnight at room temperature, the precipitate was removed by filtration. The ether was removed from the filtrate, and the residue was filtered to remove a small remaining amount of the precipitate. The filtrate was then distilled to give the corresponding esters of the carboxylic acid. The results are summarized in Table 2.

Phosphorylation of Ethanol by Means of Triphenyl Phosphine, Diethyl Azodicarboxylate, and Phenyl Dihydrogen Phosphate. A solution of triphenyl phosphine (2.62 g, 0.01 mol) in 10 m*l* of tetrahydrofuran was added drop by drop, into a solution of phenyl dihydrogen phosphate (1.74 g, 0.01 mol), diethyl azodicarboxylate (1.74 g, 0.01 mol), and ethanol (1 m*l*) in 15 m*l* of tetrahydrofuran, under vigorous stirring at room temperature. After the solution had been kept standing overnight at room temperature, aniline (0.93 g, 0.01 mol) was added to it. The anilinium phenyl hydrogen phosphate (0.80 g, 30% recovered, mp 170—184°C, R_f 0.14; solvent, isopropyl alcohol, concd. NH_4OH, H_2O=8 : 1 : 1) thus formed was removed by filtration. The filtrate was evaporated to dryness under reduced pressure, and the residue was treated with 5 m*l* of benzene. The undissolved diethyl hydrazodicarboxylate (1.28 g, 72.7%, mp 130—135°C) was then removed by filtration, and the filtrate was extracted with water (10 m*l*×3). The aqueous layer was evaporated to dryness to give anilinium phenyl ethyl phosphate (1.33 g, 45.0%, mp 78—92°C), which was then recrystallized from ethyl acetate, mp 97—99°C. The benzene layer was evaporated to dryness to give triphenyl phosphine oxide (2.81 g, mp 110—145°C), which was then recrystallized from carbon tetrachloride (mp 155°C).

Found: C, 56.70; H, 6.27; N, 4.76%. Calcd for $C_{14}H_{18}NO_4P$: C, 56.94; H, 6.15; N, 4.74%.

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