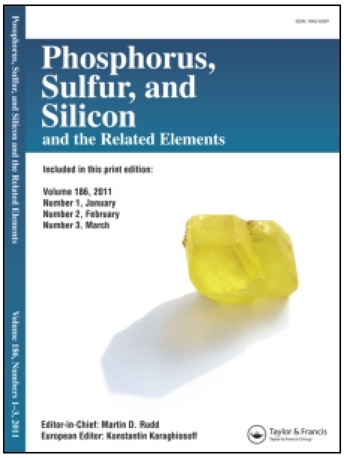

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ORGANOPHOSPHORUS COMPOUNDS XXXIX. THE ACTION OF ALKYL PHOSPHITES ON OXAZOLIDINEDIONES. A NOVEL SYNTHESIS OF CARBAMIC ACID DERIVATIVES

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ORGANOPHOSPHORUS COMPOUNDS XXXIX. THE ACTION OF ALKYL PHOSPHITES ON OXAZOLIDINEDIONES. A NOVEL SYNTHESIS OF CARBAMIC ACID DERIVATIVES

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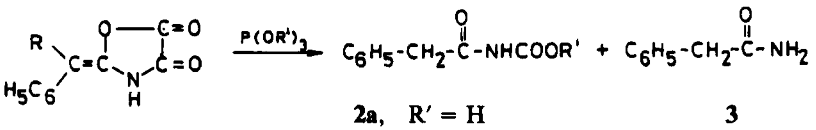
Depending upon the experimental conditions trimethyl-, triethyl-, and triisopropyl phosphites react with oxazolidinedione (**1a**) to give acid **2a** and/or the corresponding alkyl ester **2b, c**. Phenylacetamide (**3**) is also formed in a small amount. On the other hand, trialkyl phosphites cause the quantitative conversion of dione **1b** into diphenylacetamide. The identity of the new compounds is established from analytical, chemical and spectroscopic evidence.

INTRODUCTION

During the course of our investigations on the reaction of alkyl phosphites with lactones and lactams,[1-3] we have now studied the behaviour of oxazolidinediones (**1a, b**) wherein both the lactone and lactam functions are incorporated, towards these phosphite esters.

RESULTS AND DISCUSSION

Trimethyl phosphite reacts with oxazolidinedione (**1a**) in toluene at the reflux temperature for 10 hrs, to give the first reported phenylacetylcarbamic acid (**2a**) and its methyl ester **2b**, along with trace amounts of phenylacetamide (**3**). When this reaction was conducted in the presence of controlled amounts of water, the reaction was markedly accelerated and goes to completion after only 4 hrs reflux. Carrying out the reaction of (**1a**) with excess of trimethyl phosphite (up to 3 mole equivalents) leads to the formation of ester **2b** as the main reaction product. Phenylacetamide (**3**) was also formed in a minor amount.



$C_6H_5-CH_2-\overset{O}{\overset{\|}{C}}-NHCOOR' + C_6H_5-CH_2-\overset{O}{\overset{\|}{C}}-NH_2$

1a, R = H
b, R = C_6H_5

2a, R′ = H
2b, R′ = CH_3
2c, R′ = C_2H_5

3

Triethyl phosphite reacts with **1a** in a manner analogous to that described above, to yield acid **2a** (yield *ca* 50%) and its ethyl ester **2c** (*ca* 40%), respectively. On the other hand, when the same reaction was carried out with triisopropyl phosphite, the yield of acid **2a** increased appreciably (*ca* 80%) while no isopropyl ester could be isolated from the reaction mixture. Dione **1a** was recovered practically unchanged when refluxed alone in toluene for 48 hrs in the absence of the phosphite reagent.

Elementary and mass spectroscopic analyses of the new acid **2a** and its methyl ester **2b** agreed with the molecular formulae $C_9H_9NO_3$ and $C_{10}H_{11}NO_3$, respectively. The nature of acid **2a** was deduced from its free solubility in 10% aqueous sodium bicarbonate solution, and from its decarboxylation to phenylacetamide (**3**), upon heating above its melting point. The fact that acid **2a** was converted into phenylacetylurea, upon treatment with thionyl chloride followed by ammonia, lends additional support to the assigned structure **2a**. Complementary evidence to structure **2a** was also gained from IR and ^1H NMR spectral data (cf. Experimental). The identity of ester **2b** was also established from compatible IR and ^1H NMR data (*vide infra*). Moreover, the primary fragmentation step of acid **2a** and its ester **2b** under electron impact proceeds in the usual manner expected for aliphatic carboxylic acids ($M—CO_2$) and the methylated ester ($M—CH_3OH$), respectively (Chart 1). In addition, the mass spectra of **2a** and **2b** show close resemblance to each other with respect to the value of the base peak (radical cation **b** at m/e 118) despite the varying mechanisms leading to its formation in each case. Thus ion **b** can arise from acid **2a** either by loss of CO_2 molecule from M^+ followed by ejection of NH_3 molecule from the produced radical cation **g**, or *via* initial rearrangement of M^+ to give ion **f** and subsequent loss of H_2NCOOH molecule from the latter ion. Formation of the base peak **b** in the spectrum of ester **2b** can be explained in term of loss of CH_3OH molecule from M^+ followed by expulsion of $HN{=}C{=}O$ molecule from the resulting radical cation **i** (m/e 161).

It seems that the reaction of **1a** with trialkyl phosphites necessitates presence of water elements in the medium is supported by the finding that since no interaction occurs in rigorously dried solvents such as benzene even after refluxing for 48 hrs. Upon addition of controlled quantities of water (up to 1% v/v) to the benzene solution, however both acid **2a** and its alkyl ester **2b** or **2c** were formed just after 8 hrs reflux.

The formation of the methyl ester **2b** along with the acid **2a** in the reaction of **1a** with trimethyl phosphite is ascribed to the facile methylation of carboxylic acids with trimethyl phosphite.[4] This is supported by the fact that acid **2a** is readily methylated when allowed to react with trimethyl phosphite in boiling toluene. The presence of phenylacetamide (**3**) in a minute amount among the reaction products of **1a** with trimethyl phosphite can be attributed to the decarboxylation of acid **2a** by the phosphite reagent which acts as a Lewis base.[5] In absence of trimethyl phospite, acid **2a** is quite stable even after boiling in toluene for 15 hrs.

It was also of interest to examine the reactivity of 2-diphenylmethyleneoxazolidine-4,5-dione (**1b**) towards trialkyl phosphites to manifest whether it would behave in a manner similar to **1a**. With trimethyl-, triethyl- and triisopropyl phosphites, the reaction proceeded in refluxing benzene yielding one and the same product in each case and in an almost quantitative yield. This latter compound which has the molecular formula $C_{14}H_{13}NO$ (as inferred from its elemental and mass spectrometric analyses) was proved to be diphenylacetamide (**5**). The formation of (**5**) can be tentatively explained on the premise that trialkyl phosphites—acting as a Lewis base[5]—catalyse the decarboxylation of the presumably formed acid **4**.

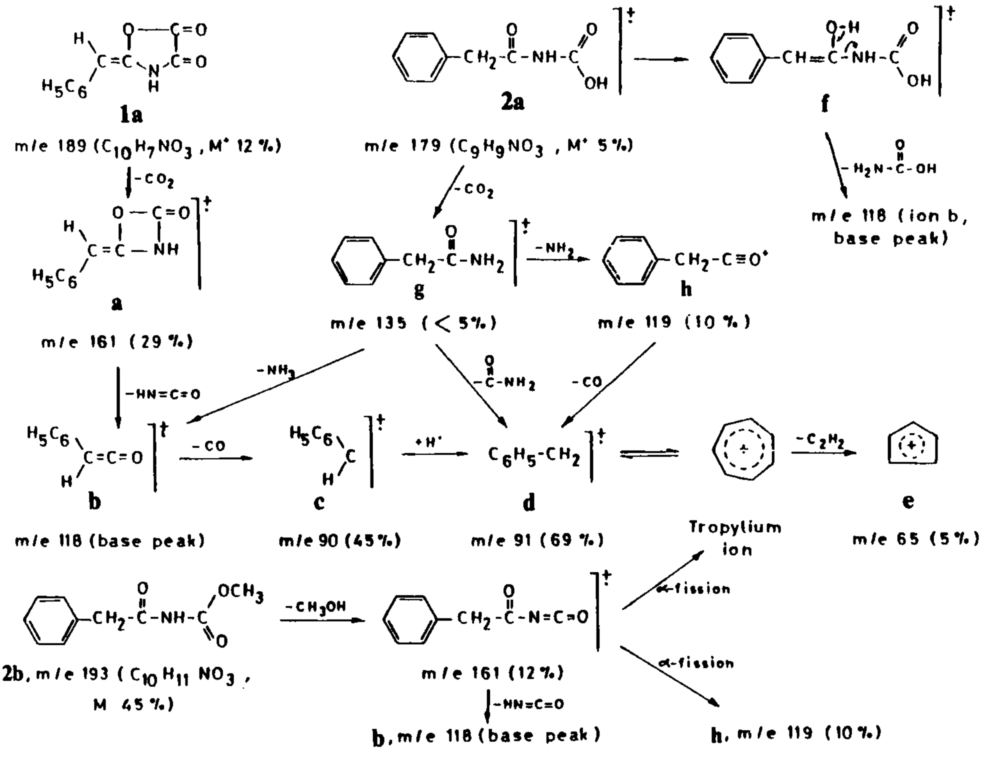
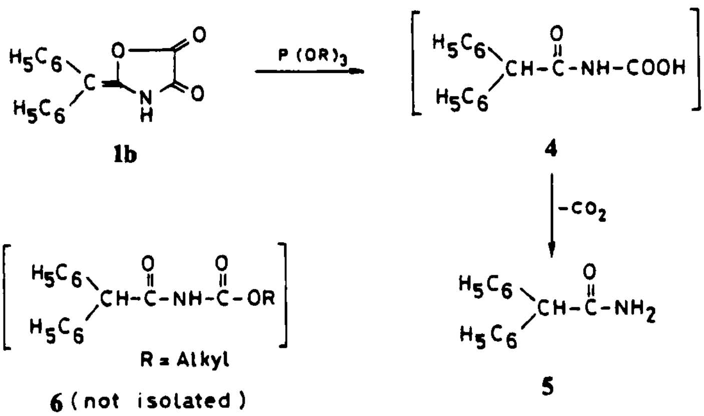


Chart (1)

The absence of esters like **6** in the reaction of trialkyl phosphites with **1b** strongly suggests that the rate of decarboxylation of intermediate **4** to give amide **5** proceeds much faster than the esterification reaction.

From the above results, it can be seen that the reaction of trialkyl phosphites with oxazolidinediones **1a, b** leads to different products depending on the structure of the dione as well as on the nature of the trialkyl phosphite used. Moreover, it is also safe to conclude that oxazolidinediones **1a, b** behave towards alkyl phosphites in a



manner markedly different from that already known with other diones, lactones and lactams. The significance of the finding of the present investigation does not limit to establishing of a new type of ring cleavage of an oxazolidinedione ring by alkyl phosphites, but extends to developing of a novel method for preparing carbamic acid derivatives (cf. **2**).

EXPERIMENTAL

All melting points are uncorrected. Petroleum ether (b.r. 40–60°C) was used in recrystallization. Trialkyl phosphites[6,7] were purified by prolonged treatment with sodium, followed by fractional distillation. The IR spectra were run on a Perkin-Elmer Infracord spectrometer Model 157G (Grating), in KBr. The ^1H NMR spectra were taken at 90 mHz on Bruker 90 instrument. The mass spectra were run at 70 eV on Kratos MS 50 equipment provided with data system. The starting diones **1a, b** were prepared by established procedures.[8]

Reaction of 1,3-oxazolidine-2-phenylmethylene-4,5-dione (**1a**) *with trimethyl phosphite.* A mixture of dione **1a** (0.56 g, 0.003 mole) and trimethyl phosphite (0.49 g, 0.004 mole) in dry toluene (20 ml) was refluxed for 10 hrs. The mixture was concentrated, cooled and the precipitate that formed was filtered then crystallized from toluene/pet. ether to give the acid **2a** as colourless crystals, m.p. 210°C, in 20% yield. Calcd. for $C_9H_9NO_3$: C, 60.03; H, 5.04; N, 7.82. Found: C, 60.10; H, 5.08; N, 7.73%. The IR spectrum of **2a** (expressed in cm^{-1}) showed bands at: 3325, 3380 (CO—NH), 1670 (CO · OH), 1620 (CO—NH), and 1460, 1480 (C=C aromatic). The ^1H NMR spectrum of **2a** in DMSO (expressed in δ scale) showed signals at: 3.61 (C_6H_5—CH_2, s), 7.70 (OH, broad, s), 10.42 (NH) and 7.30 (5 aromatic protons, m).

The filtrate was evaporated under reduced pressure, and the residue left was triturated with pet. ether and crystallized from ether/pet. ether to give the ester **2b** as colourless crystals, m.p. 145°C (70%). Calcd. for $C_{10}H_{11}NO_3$: C, 62.12; H, 5.70; N, 7.25. Found: C, 62.19; H, 5.68; N, 7.29%. The IR spectrum of **2b** (expressed in cm^{-1}) showed bands at: 3170, 3230 (CO—NH), 1740 (CO-ester), 1680 (CO—NH), and 1500, 1550 (C=C aromatic). The ^1H NMR of **2b** in $CDCl_3$ (expressed in δ scale) showed signals at: 4.00 (C_6H_5—CH_2, s), 3.77 (CH_3-ester, s), 10.00 (NH) and 7.33 (5-aromatic protons, m). Phenylacetamide (**3**)[9] was detected in the ether/pet. ether filtrate by t.l.c.

On repetition of the above experiment in the presence of a few drops of water, the reaction was accelerated and completed after 4 hrs to give the same results.

Reaction of oxazolidinedione (**1a**) *with excess trimethyl phosphite.* A mixture of dione **1a** (0.56 g, 0.003 mole) and trimethyl phosphite (1.47 g, 0.012 mole) in toluene (20 ml) was refluxed for 12 hrs, then concentrated. On addition of petroleum ether, the ester **2b** was precipitated (80%). Phenylacetamide (**3**) was detected in the filtrate by t.l.c.

Reaction of **1a** *with triethyl phosphite.* In a similar manner, dione **1a** reacted with triethyl phosphite and working up as described in case of trimethyl phosphite gave the acid **2a** (m.p., mixture m.p. and comparative IR spectra) (in a 40% yield) and the ethyl ester **2c** as colourless crystals; crystallized from ether/petr. ether, m.p. 100°C (in a 40% yield). Calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.28; N, 6.76. Found: C, 63.79; H, 6.30; N. 6.69%. The IR spectrum of **2c** (expressed in cm^{-1}) showed bands at: 3180, 3240 (CO—NH), 1750 (CO-ester), 1690 (CO—NH), 1500, 1550 (C=C aromatic). The ^1H NMR of **2c** in DMSO (expressed in δ scale) showed signals at: 1.20 (CH_2—CH_3, t), 3.80 (C_6H_5—CH_2, s), 4.10 (CH_2—CH_3, q), 10.80 (NH, s) and 7.30 (5 aromatic protons, m).

The reaction of triisopropyl phosphite with **1a** under a similar condition gave the acid **2a** in a 65% yield. Phenylacetamide (**3**) was also detected in this case by t.l.c.

Stability of dione **1a** *in refluxing toluene.* Dione **1a** (0.56 g, 0.003 mole) was refluxed in toluene (20 ml) for 48 hrs. After cooling, the precipitate that formed was collected and crystallized from acetone to give dione **1a** in a 98% yield (identified by m.p., mixture m.p. and comparative IR spectra with an authentic sample.[8]

Pyrolysis of the acid **2a**. Acid **2a** (0.28 g, 0.0015 mole) was heated at 220°C (bath temperature) for two minutes and cooled. The product that left was crystallized from benzene to give phenylacetamide (**3**) (identified by m.p., mixture m.p. and comparative IR spectra with an authentic sample).[9]

Formation of phenylacetylurea. To a solution of the acid **2a** (0.56 g, 0.003 mole) in dry benzene (50 ml) was added 3 ml of thionyl chloride. The mixture was refluxed on a steam bath for 3 hrs. The volatile materials were removed under reduced pressure and the oily residue that left behind was washed several times with dry benzene then evaporated till dryness. Dry ether (100 ml) was added then dry ammonia vapour was passed for 30 minutes in the solution under cooling. The precipitate that formed was collected and crystallized from dioxane-ethanol (2 : 3) to give phenylacetylurea (65%) (verified from m.p., mixture m.p. and comparative IR spectra with an authentic sample).[10]

Reaction of dione **1a** *with trimethyl phosphite in benzene.* A mixture of dione **1a** (0.56 g, 0.003 mole) and trimethyl phosphite (0.49 g, 0.004 mole) in dry benzene (30 ml) was refluxed for 48 hrs. On cooling, dione **1a** was precipitated in a quantitative yield and identified (m.p., mixed m.p. and comparative IR spectra).

On repetition of the same experiment in the presence of a few drops of water, the reaction was completed after 8 hrs. After cooling and working up as described before, the acid **2a** and its methyl ester (**2b**) were isolated in 20% and 60% yields, respectively, and identified by m.p. and mixed m.p. determination with corresponding reference samples.

Methylation of the acid **2a.** A mixture of acid **2a** (0.34 g, 0.002 mole) and trimethyl phosphite (0.49 g, 0.004 mole) in toluene (20 ml) was refluxed for 10 hrs. The mixture was concentrated and on addition of petroleum ether, the ester **2b** was precipitated in an 80% yield and identified (m.p., mixture m.p. and comparative IR spectra). Phenylacetamide (**3**) was detected in the filtrate by t.l.c.

Reaction of 2-diphenylmethyleneoxazolidine-4,5-dione (**1b**) *with trimethyl phosphite.* A mixture of dione **1b** (0.53 g, 0.002 mole) and trimethyl phosphite (0.36 g, 0.003 mole) in benzene (acetonitrile or methylene chloride) (30 ml), was refluxed for 8 hrs. The volatile materials were removed *in vacuo*. The oily residue that left was triturated with petroleum ether till solidified and the precipitate was collected then crystallized from aqueous ethanol to give diphenylacetamide (**5**) (80%), which was identified by m.p., mixture m.p. and comparative IR spectra with an authentic sample).[11]

Similarly, diphenylacetamide (**5**)[11] was isolated in 75% and 70% yield, respectively from the reaction of dione **1b** with triethyl- and triisopropyl phosphites.

When dione **1b** was refluxed alone in benzene, acetonitrile or methylene chloride for 48 hrs, it was recovered unchanged in a quantitative yield and identified (m.p., mixed m.p. and comparative IR spectra).

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