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REACTIONS OF AZIDES WITH α-ESTER PHOSPHORUS YLIDS

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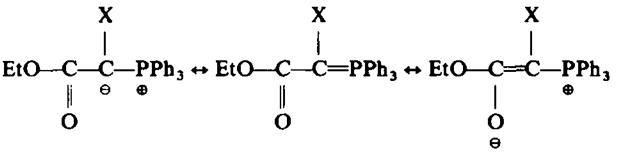
Abstract—The reactions of α-ester phosphorus ylids with several azides are described together with a kinetic investigation. The two reaction courses, leading either to diazo compounds or to vic-triazoles,are interpreted as proceeding by an addition elimination sequence. The low values of the entropies of activation provide evidence for a concerted addition in the first step of the reaction.

INTRODUCTION

α-Ester phosphorus ylids (I) are commonly represented in three resonance forms (Ia, b and c) and can, a priori, react with azides either as carbanions (Ia) or as unsaturated systems C=P (Ib) and C=C (Ic).



$$\mathrm{EtO{-}\underset{\underset{O}{\|}}{C}{-}\overset{\overset{X}{|}}{\underset{\ominus}{C}}{-}\overset{\oplus}{P}Ph_3 \leftrightarrow EtO{-}\underset{\underset{O}{\|}}{C}{-}\overset{\overset{X}{|}}{C}{=}PPh_3 \leftrightarrow EtO{-}\underset{\underset{O^{\ominus}}{|}}{C}{=}\overset{\overset{X}{|}}{C}{-}\overset{\oplus}{P}Ph_3}$$

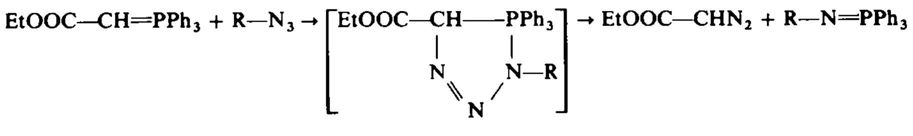
Ia Ib Ic

X = H, Me

A previous investigation, carried out with ethyl azidoformate,[1] indicated that two reaction schemes can occur, leading either to diazo compounds and iminophosphoranes (when X = H), or to *vic*-triazoles and triphenylphosphine oxide (X = Me). The reaction of I (X = H, Me) with tosyl azide,[2] afforded only the diazo compounds and tosyliminotriphenylphosphorane. In the present work the reactions of carbethoxymethylenetriphenylphosphorane (I, X = II) and carbethoxyethylidenetriphenylphosphorane (I, X = Me) with several azides, belonging to different classes, are examined. A kinetic study is also presented in order to elucidate the reaction mechanism.[3]

RESULTS AND DISCUSSION

Product studies. m-Nitrobenzoyl azide, phenyl azide and diphenylphosphorazidate were allowed to react with an equimolecular amount of carbethoxymethylenetriphenylphosphorane (I, X = H) in methylene chloride at room temperature. The reaction conditions and yields of the two expected products III and IV are summarized in Table 1. Ethyl diazoacetate (III) was identified by its IR[4] (=CH at 3090 cm^{-1}, CN_2 at 2100 cm^{-1} and C=O at 1695 cm^{-1}) and NMR spectrum ($CDCl_3$, =CH sharp singlet at δ 4·82, a methylene quartet at δ 4·22 and a Me triplet at δ 1·25). The iminophosphoranes (IV) were characterized by comparison with authentic samples



II III IV

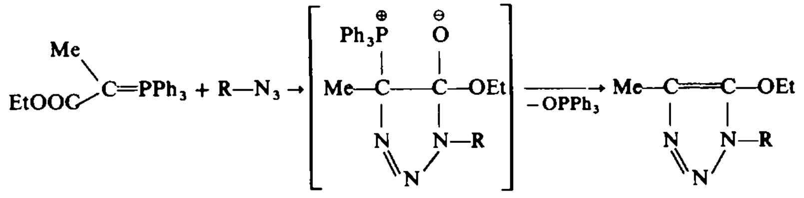
TABLE 1. REACTION OF I (X = H) WITH AZIDES

Azide	Reaction time at room temp	Ethyl diazoacetate yield, % *a*	*b*	Iminophosphorane yield, %	recrystn solvent	m.p.	$\nu_{P=N}$ cm^{-1}
m-NO_2—C_6H_4—CO—N_3	3 hr	69	40	60	ethyl acetate	156·5–8	1330
C_6H_5—N_3	4 days	15	10	30	ether	136·5–7	1340
$(C_6H_5O)_2PO$—N_3	1 day	84	58	85	ethyl acetate	147–9	1320

[a] determined by IR spectroscopy, [b] Isolated by distillation under reduced pressure.

prepared from triphenylphosphine and the respective azides (Staudinger reaction).[5] The IR spectra of IV showed typical P=N bands at ca. 1330 cm^{-1} and P—C bands at 1430, 1110 and 990 cm^{-1}.[6] The reaction of diphenylphosphorazidate with I (X = H) afforded, in addition to III and IV, a small amount (ca. 7%) of diphenylphosphoramidate, m.p. 153°.

When X in I is Me instead of H, the reaction with acyl azides followed a different course, leading to 1-acyl-4-methyl-5-ethoxy-1,2,3-triazoles (VI) and triphenylphosphine oxide. Table 2 gives a summary of our results with mono- and bis-acyl azides.



V VI

The mono- and bis-triazoles were characterized by IR and NMR spectroscopy and by elemental analysis. The IR spectra show typical C=O bands in the region 1700–1720 cm^{-1} (strong) and C—O—C streching vibrations at 1250 (strong) and 1025 cm^{-1} (medium). The NMR spectra ($CDCl_3$) exhibited a CH_3—C=C sharp singlet at ca. δ 2·30, a methylene quartet at ca. δ 4·45 and a Me triplet at ca. δ 1·45. The different behaviour of carbethoxymethylenetriphenylphosphorane and carbethoxyethylidenetriphenylphosphorane in their reaction with acyl azides is very unusual since contribution of the betaine structure (Ic) to the ground state structure of the ylid, as evidenced by the displacement of the C=O band in the IR spectra (at 1605 and 1625 cm^{-1} respectively), is nearly the same for both α-ester ylids and inferior to that of α-keto ylids (at ca. 1520 cm^{-1})[7] which are known to give exclusively *vic*-triazoles.[2] The exact

TABLE 2. MONO- AND BIS-1-ACYL-4-METHYL-5-ETHOXY-1,2,3-TRIAZOLES

Triazole VI R	Reaction conditions	Yield %	Recrystn. solvent	m.p. °C	Anal. data (Calc./Found) C	H	N	O
C_6H_5—CO—	2 months, 20°	63	methanol	87–88	62·34/62·20	5·63/5·65	18·18/18·40	13·85/13·95
m-NO_2—C_6H_4—CO—	1 day, 20°	73	methanol	92–94·5	52·17/52·31	4·35/4·26	20·29/20·24	23·19/23·06
p-NO_2—C_6H_4—CO—	2 days, 20°	77	chloroform-n-hexane	119–120·5	52·17/52·15	4·35/4·50	20·29/20·35	23·19/23·20
p-MeO—C_6H_4—CO—	15 days, 40°	60–70	ether	84–85	59·77/59·56	5·75/5·70	16·09/15·93	18·39/18·26
m-CO—C_6H_4—CO—	3 months, 20°	73	methanol	119–121	56·25/56·41	5·20/5·35	21·88/21·69	16·67/16·71
p-CO—C_6H_4—CO—	3 months, 20°	73	methanol	166–168	56·25/56·37	5·20/5·32	21·88/21·77	16·67/16·72

reason for this different behaviour remains obscure. This phenomenon was also observed for ethyl azidoformate,[1] but not for tosyl azide.[2,*]

Kinetics. The reactions leading to diazo compounds or triazoles are interpreted as proceeding via the intermediates II and V. Fragmentation of II is comparable with the decomposition of some unstable triazolines,[8] and the mode of decomposition of V is similar to the second step in the well known Wittig reaction.[9] IR examination of the reaction of I (X = H) with azides shows that the diazo band at 2100 cm^{-1} appears simultaneous with the disappearance of the azide band, indicating that II decomposes as soon as it is formed. An accumulation of intermediate V, which has escaped any isolation, is also unlikely. The first step in both reaction schemes are thus rate determining and the kinetics can be easily studied by following the disappearance of the azide absorption band in the IR spectrum. The rate data for two typical systems, using equimolecular concentrations of ylid and azide in benzene solution, agree with a second order reaction rate. The rate constants, determined at different temperatures, and the activation parameters are listed in Table 3. The low values of the entropies of activation suggest a concerted cycloaddition of the azides onto the C=P and C=C bonds of the ylids. The values are comparable with those reported for cycloadditions of azides to dipolarophiles.[10] Our results are not consistent with the two-step reaction path proposed[2] for the formation of the cyclic intermediates. According to this author, the reaction occurs by nucleophilic attack of the ylid carbanion (Ia) on the terminal N atom of the azide to give a triazene (VII) followed by ring closure. This proposal is unlikely in view of the observed low entropy values.

TABLE 3. RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE REACTIONS OF I(X = H, Me) WITH AZIDES IN BENZENE

Ylid	Azide	$\nu_{as}N_3$ cm^{-1}	T °C	$10^3 k_2$ sec^{-1} l mole^{-1}	ΔE kcal mole^{-1}	ΔS* e.u.
EtOOC—CH=PPh$_3$	(PhO)$_2$PO—N$_3$	2170	25	1·69	12·4±0·1	−31·5
			30·0	2·45		
			35·0	3·35		
			40·0	4·80		
			50·0	8·70		
EtOOC—CMe=PPh$_3$	*m*-NO$_2$C$_6$H$_4$CO—N$_3$	2140	5·0	0·91	9·4±0·1	−40·6
			25·0	2·82		
			30·0	3·70		
			35·0	4·67		
			40·0	5·97		

Qualitative observations of reactivity clearly show the rate enhancement with a stronger electronegative azide and indicate a charge distribution in the transition states, as pictured in VIII and IX respectively.

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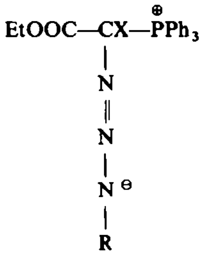
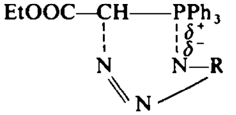
[*] In view of the above results and the fact that 1-tosyl-5-ethoxy-1,2,3-triazole is known to undergo ring opening to the corresponding diazo compound (P. Grünanger, P. Vita Finzi and C. Scotti, Chem. Ber., 98, 623 (1965)), we reinvestigated the reaction of I (X = Me) with tosyl azide, but our results led to the same conclusion as Harvey's.[2] The infrared spectrum of the reaction mixture, after complete reaction, showed a C=O band at 1740 cm^{-1} and a P=N band at 1145 cm^{-1}.

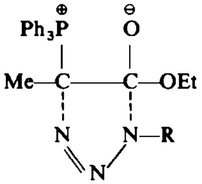


$\mathrm{EtOOC{-}CX(-N{=}N{-}N^{\ominus}{-}R){-}\overset{\oplus}{P}Ph_3}$

VII



VIII



IX

The reactions studied here fit into the general class of 1,3-dipolar addition reactions of azides to dipolarophiles, being a concerted process in which both new σ-bonds are formed simultaneously, but not at equal rates.[11]

EXPERIMENTAL

M.ps were obtained on a Leitz apparatus. IR spectra were taken on a Perkin-Elmer 521 spectrometer. NMR spectra were recorded with a Varian A-60 spectrometer using TMS as an internal reference.

Phosphorus ylids. The ylids used were prepared by treating the respective phosphonium salts with NaOH (salt method).[12] The m.ps, after two recrystallizations from EtOAc and careful drying, were found to be higher than those reported:[12] 129–130·5° for I, X = H (reported, 116–117°) and 160–162° for I, X = Me (reported 156–157°).

Reaction of carbethoxymethylenetriphenylphosphorane with azides. 0·02 mole ylid (7·0 g) was treated with 0·02 mole azide in 100 ml CH_2Cl_2 at room temp. After completion of the reaction, the solvent was removed and the residue treated with ether in order to precipitate the iminophosphorane. The mother liquor was concentrated and the residue distilled under reduced press to give ethyl diazoacetate.

When the reaction mixture of I (X = H) and diphenylphosphorazidate was saturated with ether and then allowed to crystallize at low temp, diphenylphosphoramidate $(PhO)_2PO{-}NH_2$, was isolated in ca. 7% yield; m.p. 153–154° (CH_2Cl_2); IR (KBr, cm^{-1}) NH_2 at 3430 and 3240, =CH at 3050, C=C at 1590 and 1490, P—O—Ph at 1210, Ph at 680 and 770; NMR ($CDCl_3$) aromatic multiplet at 7·1–7·4, NH_2 at ca. 5·3 (can be exchanged with D_2O).

Synthesis of iminophosphoranes by the Staudinger method. Equimolecular amounts of triphenylphosphine and azide were mixed in ether solution at room temp. N_2 evolution was observed and the iminophosphorane precipitated from the mixture; yields were 76% with *m*-nitrobenzoyl azide and 92% with diphenylphosphorazidate. The third imonophosphorane, phenyliminotriphenylphosphorane, was described by Staudinger.[5a]

Reaction of carbethoxyethylidenetriphenylphosphorane with acyl azides. 0·02 mole ylid (7·2 g) was treated with 0·02 mole mono-azide or 0·01 mole bis-azide in 100 ml CH_2Cl_2 or benzene at the appropriate temp. After complete reaction (IR monitor) the solvent was removed under reduced press and the residue fractionally crystallized from MeOH (except for 1-*p*-methoxybenzoyl-4-methyl-5-ethoxy-1,2,3-triazole which was isolated from ether). All the fractions were characterized by their IR spectrum.

Triphenylphosphine oxide was isolated in high yield (70–80%) when the residue was fractionally crystallized from EtOAc or ether: m.p. 154–155°. Its IR spectrum showed the following absorptions: $=$C—H at 3040, C$=$C at 1590 and 1480, C—P at 1435, 1115 and 990, P$=$O at 1185, Ph at 540, 690, 715 and 750 cm^{-1}.

Kinetic measurements. Equimolecular mixtures of ylid and azide were accurately weighed and dissolved in benzene. The two solns were allowed to come separately to thermal equilibrium in the thermostat and then mixed. The reaction was followed spectrometrically, using the intensity of the azide absorption band. Azide concentrations were determined from the observed absorption using a calibration curve. By plotting 1/(azide) *vs* time, linear plots up to high degree of conversion (70–80%) were obtained. The second order constants were determined from the slopes of the linear plots. Measurements were made at several temps and the energies of activation were determined graphically from log k_2 *vs* 1/T. The entropies of activation were calculated from the rate constants at 25·0° using the following equation:

$$\Delta S^{*} = 4{\cdot}576 \log k_2 (\mathrm{sec}^{-1}\ \mathrm{l\ mole}^{-1}) - 49{\cdot}14 - 4{\cdot}576 \log T + \Delta E/T.$$

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