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TETRAZOLO-AZIDO ISOMERIZATION IN HETEROAROMATICS—III[1]

THE STAUDINGER REACTION OF TETRAZOLOPYRIDINES WITH TRIPHENYL PHOSPHINE

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Abstract—The reactions of tetrazolopyridines and 4-azidopyridine 1-oxide with triphenylphosphine to form iminophosphoranes have been studied kinetically in various solvents. The mechanisms for the formations of the products are proposed and discussed.

IT IS WELL known that most covalent azides react with triphenylphosphine and other trivalent phosphorous compounds to give nitrogen and iminophosphoranes.[2] The rate measurements have disclosed the reactions of triphenylphosphine with aryl azides to be of second order over-all, and to be accelerated by electron-withdrawing *meta* or *para* substituents in the azides.[3]

Recently, Zhmurova *et al.*, have reported the reactions of tetrazoles with triphenylphosphine.[4] Kirmse has suggested the mechanism for the formation of 2-(triphenylphosphoranyliden)aminopyridine to be *via* a pyridyl nitrene.[5] However, no report is available on the reaction mechanism.

As a continuation of our previous report on the tetrazolo-azido isomerization, and photochemical and thermal reactions of tetrazopolyazine and tetrazolopyridines,[6] this paper deals with the Staudinger reaction of substituted tetrazolopyridines with triphenylphosphine compared to that of 4-azidopyridine 1-oxide.

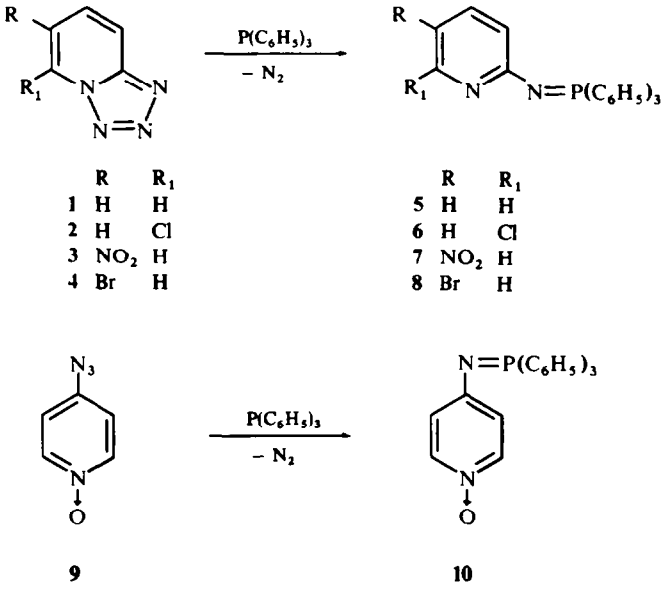
RESULTS AND DISCUSSION

Reactions of tetrazolo[1.5-a]*pyridines and 4-azidopyridine 1-oxide with triphenylphosphine*

The reactions of tetrazolo[1.5-a]pyridines (**1**, **2**, **3** and **4**), and 4-azidopyridine 1-oxide (**9**) with triphenylphosphine in various solvents at room temp and at reflux temp afforded the iminophosphorane derivatives **5**–**8** and **10** (Table I and Scheme I). The structures were confirmed by the IR, NMR and UV spectral comparison with those of a known compound (**5**)[4, 5] and by their analytical data.

Kinetic study of the reactions of tetrazolo[1.5-a]*pyridines with triphenylphosphine*

With a view to obtaining kinetic information on the above-mentioned reactions, the reactions of substituted tetrazolopyridines with triphenylphosphine were investigated in $CHCl_3$ and in DMSO. The rate measurements by UV spectra are summarized in Table III.



	R	R_1
1	H	H
2	H	Cl
3	NO_2	H
4	Br	H

	R	R_1
5	H	H
6	H	Cl
7	NO_2	H
8	Br	H

9 **10**

SCHEME 1

TABLE 1. REACTIONS OF TETRAZOLOPYRIDINES AND 4-AZIDOPYRIDINE 1-OXIDE WITH TRIPHENYLPHOSPHINE IN VARIOUS SOLVENTS

Compound No.	Solvent	Temp	Time hr	Products		
				Compound No.	Yield (%)	m.p.
1	$CHCl_3$	60	19	**5**	23	131–132
	C_6H_5Cl	110	1·3		90	
	DMSO	115	2·0		93	
2	$CHCl_3$	25	0·25	**6**	99	151–153
	DMSO	25	0·25		95	
3	$CHCl_3$	25	0·25	**7**	75	221–223
		60	0·5		96	
	MeOH	25	1·5		54	
		60	1·5		58	
	MeCN	50	1·5		56	
	DMSO	25	0·25		76	
4	$CHCl_3$	60	4·0	**8**	33	168–170
	C_6H_6	80	0·5		81	
	C_6H_5Cl	110	1·0		89	
	DMSO	115	2·0		94	
9	$CHCl_3$	25	0·5	**10**	99	202–207
	DMSO	25	0·5		99	
	MeOH	25	0·5		99	

TABLE II. SPECTRAL AND ANALYTICAL DATA OF TRIPHENYLPHOSPHORANYLIDEN-AMINOPYRIDINES

Compound No.	UV EtOH $\lambda_{max}(\varepsilon)$	NMR τ ($CDCl_3$)	Analyses (%) Found (Calcd.)		
			C	H	N
1	223 ($2{\cdot}68 \times 10^4$) 310 ($6{\cdot}10 \times 10^3$)	2·01–2·07 (17H. m. $C_6H_5 \times 3$ H_4 and H_6) 3·12 (1H. q. H_3) 3·60 (1H. td. H_5)	77·68 (77·95)	5·37 (5·40)	7·72 (7·91)
2	222 ($1{\cdot}44 \times 10^4$) 252 ($8{\cdot}36 \times 10^3$ 308 ($4{\cdot}21 \times 10^3$)	2·00–2·93 (16H. m. $C_6H_5 \times 3$. H_4) 3·27 (1H. q. H_3) 3·65 (1H. q. H_5)	71·33 (71·05)	4·63 (4·40)	7·52 (7·21)
3	208 ($3{\cdot}05 \times 10^4$) 370 ($2{\cdot}00 \times 10^4$)	1·30 (1H. d. H_6) 1·93 (1H. q. H_4) 2·0–2·6 (15H. m. $C_6H_5 \times 3$) 3·16 (1H. d. H_3)	69·19 (69·17)	4·65 (4·54)	10·55 (10·52)
4	224 ($2{\cdot}50 \times 10^4$) 259 ($1{\cdot}50 \times 10^4$) 301 (5.20×10^3)	2·30–2·70 (17H. m. $C_6H_5 \times 3$. H_4 and H_6) 3·18 (1H. d. H_3)	63·85 (63·75)	4·19 (4·19)	6·31 (6·47)
9	313 ($2{\cdot}36 \times 10^4$)	2·05–2·90 (17H. m. $C_6H_5 \times 3$. H_2. H_6) 3·58 (2H. q. H_3. H_5)	74·45 (74·60)	5·42 (5·14)	7·27 (7·57)

Second-order kinetics were observed in all runs, and the rate constants for the reactions of **1** and **4** with triphenylphosphine in DMSO were calculated as given in Table III and the rate ratios of compounds **4**/**1** become 25·6 at 97° and 36·1 at 110°, respectively. The reaction of **3** with triphenylphosphine in DMSO proceeded even at room temp. although the azido tautomer of **3** is not observed at 25° in DMSO by NMR.[6]

Furthermore, it was pointed out that the rate of the reaction of substituted tetrazolo[1,5-a]pyridine with triphenylphosphine in $CHCl_3$ was accelerated by the 6-nitro group (**3**) more than the 5-chloro group (**2**) (Table III). Whereas, the rate enhancements in $CHCl_3$ and DMSO for **2** were not observed although the equilibrium constants (K_T) of **2** were calculated to be 2·51 at 25° in DMSO and 18·0 at 23° in $CHCl_3$ respectively.

By contrast, the rates of the reactions of **3** with triphenylphosphine were 15·8 at 25° and 17·4 at 30° by changing the solvents from DMSO to $CHCl_3$, indicating the

TABLE III. THE REACTION RATES OF TETRAZOLO[1,5-a]PYRIDINES AND 4-AZIDOPYRIDINE 1-OXIDE WITH TRIPHENYL PHOSPHINE

Compound No.	Solvent	Temp	Second-order rate constants* k (M^{-1} sec^{-1})
1	DMSO	97 ± 0·3	$5{\cdot}94 \times 10^{-4}$
		105 ± 0·3	$8{\cdot}47 \times 10^{-4}$
		110 ± 0·5	$1{\cdot}06 \times 10^{-3}$
2	DMSO	25 ± 0·1	$6{\cdot}07 \times 10^{-2}$
		27 ± 0·1	$6{\cdot}72 \times 10^{-2}$
		30 ± 0·1	$7{\cdot}75 \times 10^{-2}$
	$CHCl_3$	25 ± 0·1	$4{\cdot}89 \times 10^{-2}$
		27 ± 0·1	$6{\cdot}06 \times 10^{-2}$
		30 ± 0·1	$8{\cdot}23 \times 10^{-2}$
3	DMSO	25 ± 0·1	$4{\cdot}09 \times 10^{-3}$
		27 ± 0·1	$4{\cdot}90 \times 10^{-3}$
		30 ± 0·1	$6{\cdot}37 \times 10^{-3}$
	$CHCl_3$	25 ± 0·1	$6{\cdot}47 \times 10^{-2}$
		27 ± 0·1	$8{\cdot}08 \times 10^{-2}$
		30 ± 0·1	$1{\cdot}11 \times 10^{-1}$
4	DMSO	70 ± 0·1	$3{\cdot}17 \times 10^{-3}$
		80 ± 0·1	$9{\cdot}07 \times 10^{-3}$
		97 ± 0·1	$1{\cdot}52 \times 10^{-2}$
		110 ± 0·1	$3{\cdot}61 \times 10^{-2}$
9	DMSO	20 ± 0·1	$5{\cdot}50 \times 10^{-1}$
		23 ± 0·1	$6{\cdot}93 \times 10^{-1}$
		25 ± 0·1	$8{\cdot}04 \times 10^{-1}$
	C_6H_6	20 ± 0·1	$7{\cdot}65 \times 10^{-2}$
		23 ± 0·1	$9{\cdot}29 \times 10^{-2}$
		25 ± 0·1	$1{\cdot}05 \times 10^{-1}$
	$CHCl_3$	20 ± 0·1	$1{\cdot}18 \times 10^{-1}$
		25 ± 0·1	$2{\cdot}00 \times 10^{-1}$
		30 ± 0·1	$3{\cdot}48 \times 10^{-1}$
	$CHCl_3 + I_2$	25 ± 0·1	$3{\cdot}35 \times 10^{-2}$

* Product Conversion with 60–80%. The rate law is expressed as eq. 1 and 2

$v = k$ [tetrazolopyridines] [triphenylphosphine] (1)

$v = k$ [4-azidopyridine 1-oxide] [triphenylphosphine] (2)

presence of the tetrazolo-azidoazomethine equilibrium in $CHCl_3$ and the exclusive existence as tetrazolo tautomer in DMSO.[6]

The rate of the reaction of 4-azidopyridine 1-oxide (9) with triphenylphosphine was measured in various solvents (DMSO C_6H_6 and $CHCl_3$); the rate constant increased

as shown in Table III. It is interesting that the addition of a very small amount of I_2 to a $CHCl_3$ solution of the mixture decreased the rate constant as seen in Table III.

The reaction mechanisms of tetrazolo[1.5-a]*pyridines and triphenylphosphine*

Tetrazolopyridine (**1**) is convertible to the pyridylnitrene *via* path **a**[5] or the azido tautomer *via* path **b**[4] which reacts further with triphenylphosphine to give 2-(triphenylphosphoranyliden)aminopyridine (**5**). However, from our experimental data the proposed explanation for the reaction mechanism seemed doubtful.

The rates of the reactions of tetrazolo[1.5-a]pyridines with triphenylphosphine were found to be dependent on the substituent, solvent and temp as described above. Both slow reaction rates and the second-order rate constants for **1** and **4** suggest that neither the azido tautomer nor the nitrene intermediate are involved in the reactions.[7]

These results are supported by the following spectral and chemical evidence. The NMR spectra for **1**, **3** and **4** lacked the ring proton signals due to the azido tautomer in the presence and in the absence of triphenylphosphine in DMSO (even at 80, 110, 140, and 150° at different time intervals and at 120° for 2 hr). Attempts to effect the thermal cycloadditions of **1**, **3** and **4** with acetylenic dipolarophiles in DMSO at room temp or at 60–100° were unsuccessful, indicating the absence of the reactive tautomeric azido forms and/or the pyridylnitrenes under these conditions.[6] Thus the reactions are concluded to proceed *via* path **c** involving either the betaine forms or the ylide forms.

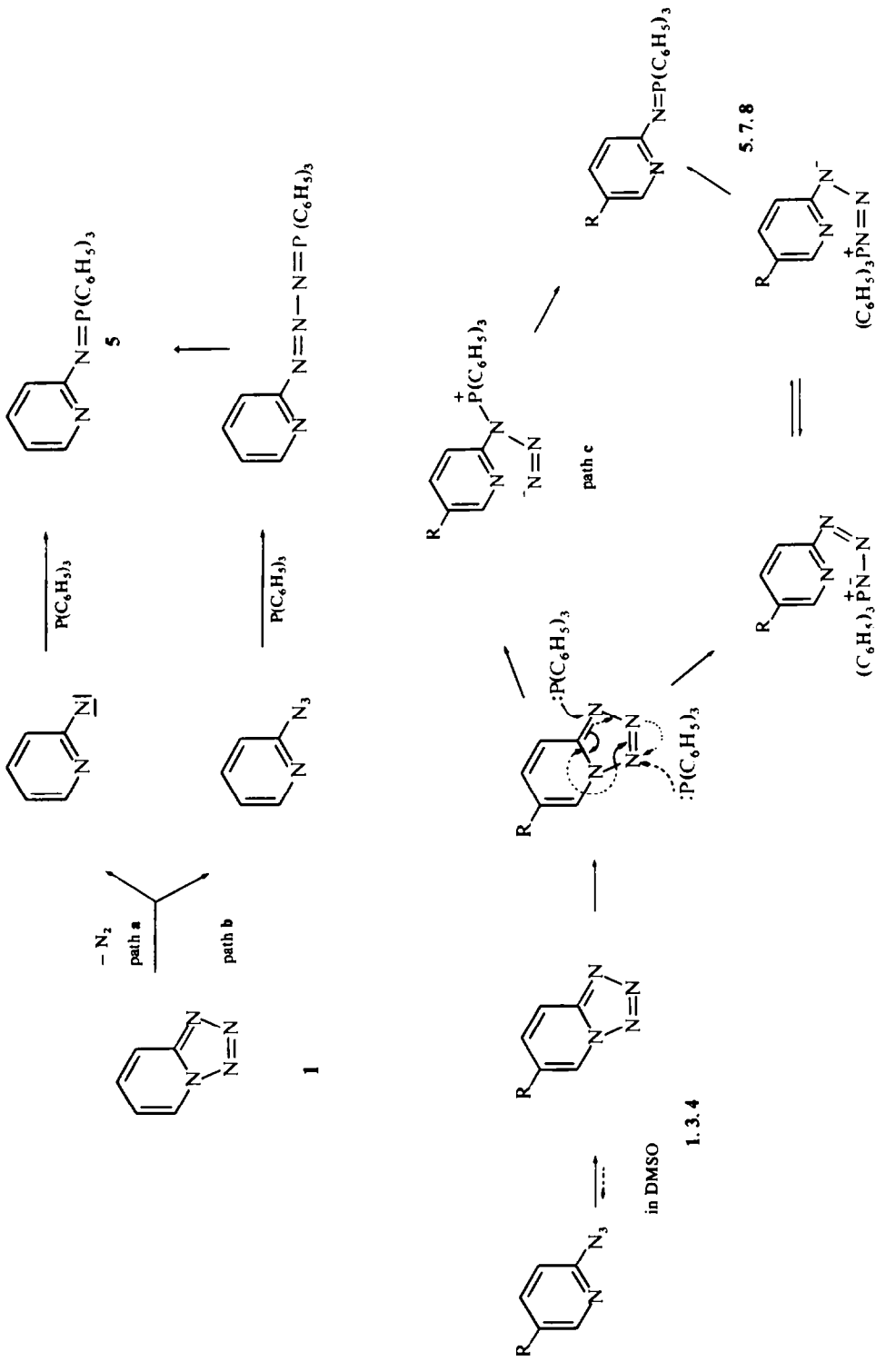
On the other hand, the reactions of **2** with triphenylphosphine in DMSO seem to proceed mainly *via* path **d**, (Scheme II), suggesting the existence of the reactive tautomeric azido form from NMR spectral data and from kinetic measurements. The proposed reaction scheme was strongly supported by agreement between the experimental results and the calculated activation in DMSO for **2** (Table IV).

In contrast the changes in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for **2**, **3** and **9** are particularly dramatic going from DMSO to $CHCl_3$ as shown in Table IV.

Thus, the mechanisms for the reactions of **2**, **3** and **9** with triphenylphosphine in $CHCl_3$ are somewhat peculiar from a kinetic point of view.

TABLE IV. ACTIVATION PARAMETERS FOR THE REACTIONS OF TETRAZOLOPYRIDINES AND 4-AZIDOPYRIDINE 1-OXIDE WITH TRIPHENYL PHOSPHINE

Compound No.	Solvent	$\Delta H^{\ddagger}$ kcal/mol	$\Delta S^{\ddagger}$ eu	$\Delta F^{\ddagger}$ kcal/mol
1	DMSO	12·5	−39·9	27·8
2	DMSO	8·8	−34·7	19·2
	$CHCl_3$	18·7	− 1·9	19·3
3	DMSO	15·9	−16·2	20·8
	$CHCl_3$	19·0	− 0·1	19·0
4	DMSO	13·5	−30·5	24·6
9	DMSO	13·7	−12·1	17·2
	C_6H_6	11·5	−24·6	18·7
	$CHCl_3$	19·9	+ 6·1	18·1


in DMSO
1.3.4
path a
path b
path c
5.7.8

SCHEME II

However. a related observation is recorded in the reaction of benzenesulphonyl azide and triphenylphosphine in $CHCl_3$ by a radical transfer mechanism *via* the ion radical Ph_3P^{+}.[8] Such a mechanism demands higher $\Delta H^{\ddagger}$ and low negative $\Delta S^{\ddagger}$ because of a high degree of the freedom in the transition states. Recently, Powell and Hall attempted to obtain the phsophinium radical cation in the reactions of triarylphosphines with electron acceptor species.[9]

Accordingly. it might be suggested that the reaction schemes for **2**, **3**. and **9** with triphenylphosphine in $CHCl_3$ proceed *via* the phosphinium radical cation intermediates such as **11** and **12**. This assumption might be supported by the fact that radical inhibitors such as I_2 retard the rate in $CHCl_3$ as described above.

EXPERIMENTAL

All m.ps were measured on a Yanagimoto micro apparatus and uncorrected. The microanalyses were performed on a Perkin-Elmer 240 Elemental Analyser. while the IR and UV spectra were obtained on a JASCO Model IR-S and a ORD/UV-5 spectrometer. respectively. The NMR spectra were recorded with a JEOL Model C-60-XL spectrometer. TMS as internal standard.

Materials

Preparations of tetrazolo[1.5-a]pyridine (**1**). 5-chloro-tetrazolo[1,5-a] pyridine (**2**). 6-nitro-tetrazolo-[1.5-a]pyridine (**3**). and 6-bromo-tetrazolo-[1.5-a]pyridine (**4**) were described in our previous report.[6] 4-Azidopyridine 1-oxide was prepared by the method of Itai and Kamiya.[10]

Reactions of tetrazolo[1.5-a]pyridines and 4-azidopyridine 1-oxide with triphenylphosphine

General method. A mixture of tetrazolo[1.5-a]pyridines (0·001 mol) and/or 4-azidopyridine 1-oxide (0·001 mol) with triphenylphosphine (0·0011 mol) in various solvents was heated in an oil bath. The solvent was evaporated *in vacuo*. and the residue purified by column chromatography, $CHCl_3$ as a eluent. which was recrystallized from MeOH to give the corresponding iminophosphorane derivatives (**5–8**. **10**) (Table I).

Kinetics

The reaction was started by the rapid addition of tetrazolo [1.5-a]pyridines to an equimolar triphenylphosphine in DMSO or $CHCl_3$. both of which had reached temp equilibrium in a thermostat. The reaction was carried out under stirring in a glass-stoppered flask as a homogeneous system. Aliquots were taken out at appropriate intervals. The reaction was stopped by dilution with EtOH. Products were determined by means of UV spectrophotometry at the maximum wavelength of the corresponding triphenyliminophosphorane derivatives. The rates of the reaction of 4-azidopyridine 1-oxide and triphenylphosphine in various solvents were measured as described above. Results are summarized in Tables III and IV.

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