Reactions of Phosphorus Compounds. 34. Preparation of Pyrazol-3-yl Ketones and Ethyl Ester from Vinyltriphenylphosphonium Bromide, Substituted Diazoacetophenones, and Ethyl Diazoacetate

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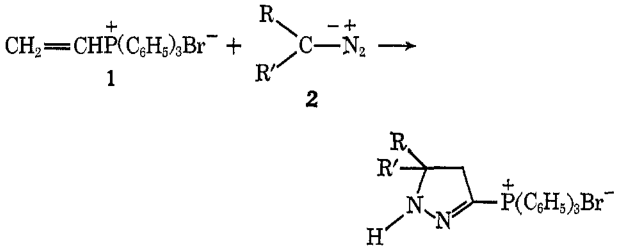
In previous papers[1,2] the preparation and reactions of 5-aryl- and 5-alkyl-substituted 2-pyrazolin-3-yltriphenylphosphonium salts (**3**) from vinyltriphenylphosphonium bromide (**1**) and substituted diazomethanes (**2**) were reported.

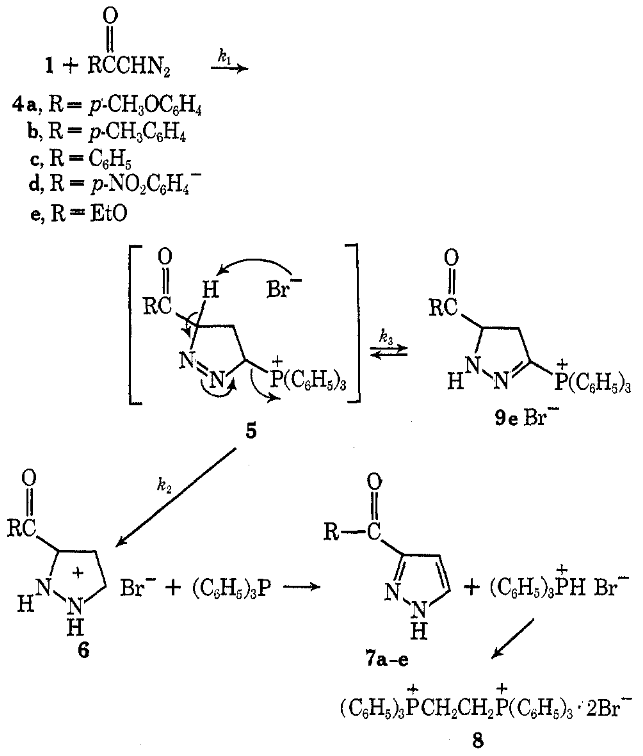


Spontaneous decomposition was observed[1] only where the 2-pyrazolinyl structure could not be formed owing to substitution α to the phosphonium moiety. The 1-pyrazolinyl species obtained from isopropenyltriphenylphosphonium bromide and diazomethane, or diphenyldiazomethane, decomposed to give 3-methylpyrazole hydrobromide and 3,3-diphenyl-1-methylallyltriphenylphosphonium bromide, respectively.[1]

In the present work, we wish to report that attempted preparation of 5-carbonyl-substituted 2-pyrazolinyltriphenylphosphonium bromides (**9**) from **1** and substituted diazoacetophenones, **4a–d**, using identical conditions with those previously reported,[1] only resulted in the isolation of pyrazol-3-yl ketones **7** and disalt **8**. The yields of **7a–e** were improved using 2 mol of vinyl salt **1** to 1 mol of **4a–e**.

The greater acidity of the 5 proton of compounds **5** compared to that of compounds **3** (where R = H, R′ = aromatic, alkyl, or H) evidently makes the rate $k_2 \gg k_3$ and none of **9** was observed. Support for this proposition is found in the fact that the lowering of the acidity of the 5 proton in compound **5e** obtained by treating ethyl diazoacetate (**4e**) with **1** allows for the conversion of **5e** to the 5-carbethoxy-2-pyrazolinyltriphenylphosphonium bromide (**9e**) in 90% yield.

Attempts to phosphonioethylate **9e**, under more vigorous conditions as described previously[2] for compounds **3**, proved to be unsuccessful, yielding only the corresponding pyrazole **7e** and disalt **8**. It has been shown[2] that phosphonioethylation of 5-substituted pyrazolines **3** is accomplished only under forcing conditions which must be greater than the conditions needed to decompose **9e** to **6e** (and thence to **7e**). Decomposition of **9e**, by heating in the absence of **1**, also gave the expected[2] 3-carbethoxypyrazole hydrobromide **6e**.



The relative rates of addition of the substituted benzoyldiazomethanes **4a–d** to the vinyl salt **1** were followed by observing the disappearance of the diazo peak (2100 cm^{-1}) in the ir. The relative rates were found by measuring the slope of the curve obtained by plotting (absorbance)$^{-1}$ *vs.* time. The relative rates (k_1) for the addition were p-MeO > p-CH$_3$ > H > p-NO$_2$ (see Table I), *i.e.*, inversely proportional to the expected stabilities of the carbanion of the 1,3 dipole. As **5d** would be expected to decompose faster than **5a**, because of the greater acidity of the α proton, the rate-determining step must be the initial formation of the 1-pyrazoline **5** from **1** and **4a–d** (k_1).

In the decomposition of the intermediate **5**, it is proposed that the bromide ion, acting as a base, removes the proton α to the carbonyl and triphenylphosphine is eliminated forming the pyrazole and triphenylphosphine hydrobromide. The triphenylphosphine hydrobromide then reacts with vinyl salt **1** to form 1,2-ethylenebis(triphenylphosphonium bromide) (**8**).[3]

Thus, it was shown that the nature of the substituent on the diazomethane dipolarophile has a profound influence on the course of the reaction.

Experimental Section

Infrared spectra were obtained on a Perkin-Elmer 137 spectrophotometer. Pmr spectra were taken on a Varian A-60A and a Perkin-Elmer R12B. The para-substituted diazoacetophenones (**4a–d**) were made by adding the appropriate acid chloride to an ether solution of diazomethane. Ethyl diazoacetate was purchased from Aldrich Chemical Co. All melting points are uncorrected.

Preparation of 3-Substituted Pyrazoles (7).—In a 100-ml flask fitted with a drying tube were placed 0.02 mol of vinyl salt, 0.01

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[1] E. E. Schweizer and C. S. Kim, *J. Org. Chem.*, **36**, 4033 (1971).

[2] E. E. Schweizer and C.S. Kim, *J.Org. Chem.*, **36**, 4041 (1971).

[3] E. E. Schweizer and R. Bach, *J. Org. Chem.*, **29**, 1746 (1964).

TABLE I

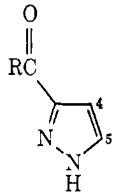
PREPARATION OF 3-SUBSTITUTED PYRAZOLES (**7a–e**) FROM VINYL SALT **1** AND SUBSTITUTED DIAZOMETHANES

Product	Ratio of **1**:**4**	Time, days	Yield, %	Yield of **8**, %	Anal. sample **7**, mp, °C	Analysis, %			Rel rate
							C	H	
7a	2:1	2	56		93–94	Calcd	65.34	4.98	50
7a	1:1	2	34			Found	64.94	5.00	
7b	2:1	2	67		130–132	Calcd	70.95	5.41	47
						Found	70.85	5.41	
7c	2:1	3	64	96	94–95[a]				26
7c	1:1	3	24	54					
7d	2:1	4	58	85	190–191	Calcd	55.30	3.25	1
						Found	55.24	3.18	
7e	2:1	1 (15)	20 (51)	55	155–157[b]				
9e	1:1	0.5	90[c]		*c*				

[a] Lit. mp 95–96°: J. Elguero and R. Jaquier, *Bull. Soc. Chim. Fr.*, 2832 (1966). [b] Lit. mp 155–157°: J. Elguero, G. Guirand, and R. Jaquier, *ibid.*, 619 (1966). [c] See Experimental Section.

TABLE II

SPECTRA OF PYRAZOLES



Product	Nmr				Ir		
	C-4	C-5	Phenyl	Other	NH	C=O	C=N
7a	6.85 (d)	7.65	6.95 (d), 8.15 (d)		3200	1630	1600
	J = 2.4 Hz		J = 8.5 Hz				
7b	6.92 (d)	7.91	7.26 (d), 7.84 (d)	CH_3O, 2.40 (s)	3150	1640	1600
	J = 2.7 Hz		J = 9.5 Hz				
7d	7.26 (d)		8.0–8.65 (m)		3250	1660	1600
	J = 2.3 Hz						

mol of the diazo compound, and 10 ml of dried chloroform. The reaction mixture was stirred for the required amount of time at room temperature, concentrated to half volume, filtered to remove 1,2-ethylenebis(triphenylphosphonium bromide), mp 285–290° (lit.[3] in A mp 297–300°), and further concentrated to an oil. This material was placed on a Florisil column (4 × 25 cm) and eluted with ethyl acetate. The first fraction (200 ml) was concentrated, petroleum ether (bp 30–60°) was added to precipitate the product, and the pyrazole was filtered and collected. The product was recrystallized from benzene–petroleum ether. The physical data are given in Tables I and II. The results of experiments run with equimolar quantities of the species **1** and **4** are also listed in Table I. Examination of the crude reaction mixture from the equimolar experiments, by nmr, shows none of the expected peaks for the intermediate **9**. The nmr shows only pyrazole **7**, disalt **8**, and some starting material **4**.

5-Carbethoxy-2-pyrazolin-3-yltriphenylphosphonium Bromide (9e).—In a three-necked 100-ml flask with a drying tube and addition funnel was placed ethyl diazoacetate (0.57 g, 0.005 mol) in 5 ml of methylene chloride. Vinyl salt (1.85 g, 0.005 mol) in 5 ml of methylene chloride was added slowly over a 12-hr period and the solution was allowed to stir for an additional 2 hr. The reaction mixture was poured into ethyl acetate and the residue was recovered by filtration. The salt was recrystallized from methylene chloride–ethyl acetate at room temperature. An analytical sample could not be obtained owing to ready decomposition. The nmr was consistent with the assigned structure: nmr ($CDCl_3$) δ 1.25 (t, 3, CH_3, J = 7 Hz), 3.25 (2 d, 2, C-4, J = 9, 12 Hz), 4.15 (q, 2, OCH_2, J = 7.0 Hz), 5.1 (dd, 1, C-5, J = 9, 12 Hz), 7.6–8.1 ppm (m, 15, phenyl).

Attempted Phosphonioethylation of 5-Carbethoxy-2-pyrazolin-3-yltriphenylphosphonium Bromide (9e).—Vinyltriphenylphosphonium bromide (0.001 mol), **9e** (0.001 mol), and 10 ml of chloroform were refluxed for 24 hr, concentrated to half volume, and filtered. The white solid collected was disalt **8** in a 73% yield. There was no phosphonioethylated product found.

Kinetic Data.—The sample for the kinetics was obtained from the reaction mixture as soon as the chloroform had been added and the mixture was homogeneous. The sample was placed in a liquid cell and the change in absorbance of the diazo peak was followed with time on a Perkin-Elmer 421 spectrophotometer. A plot of the reciprocal of the absorbance *vs.* time in minutes gave the straight-line plot. The relative rates reported are the slopes of these plots.

Pyrolysis of 5-Carbethoxy-2-pyrazolin-3-yltriphenylphosphonium Bromide (9e).—In an nmr tube some of **9e** was heated to a melt for 5 min. $CDCl_3$ was added and an nmr was taken. The pyrazole hydrobromide could not be isolated pure but the nmr was consistent with that of a sample prepared from **7e** (Table I): nmr ($CDCl_3$) δ 1.35 (t, 3, CH_3, J = 7 Hz), 4.4 (q, 2, DCH_3 J = 7 Hz), 6.95 (d, 1, C-4, J = 2.8 Hz), 8.05 (d, 1, C-3, J = 2.8 Hz), 10 ppm (s, 2, NH solvent dependent, exchanges with D_2O).

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Registry No.—**1**, 5044-52-0; **4a**, 6832-17-3; **4b**, 4250-01-5; **4c**, 3282-32-4; **4d**, 4203-31-0; **4e**, 623-73-4; **7a**, 19854-93-4; **7b**, 40711-94-2; **7c**, 19854-92-3; **7d**, 40711-96-4; **7e**, 5932-27-4; **8**, 1519-45-5; **9e**, 40711-97-5.

Kinetic Evidence for the Existence of a 1,4 Dipole

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Recently we presented experimental evidence for the rearrangement of a proposed 1,4 dipole (**1**), gen-