α,β-Unsaturated Carboxylic Acid Derivatives. X. The Synthesis and Reaction of α-Azido-diethoxyphosphinyl-α- and β-alkenes[1)]

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α,β-Dibromo-β-diethoxyphosphinylalkane (**2**) was obtained as a stereo-isomeric mixture (erythro : threo= 50 : 50) by the bromination of β-diethoxyphosphinyl-α-alkene, composed of the *E*-isomer and the *Z*-isomer (50 : 50). It was found that the reaction of **2** with sodium azide proceeded stereoselectively to give only the *E*-isomer of α-bromo-β-diethoxyphosphinyl-α-alkene, which could then be converted into α-azido-β-diethoxyphosphinyl-α-alkene (**4**), and α-azido-β-diethoxyphosphinyl-β-alkene, whose configuration was determined by the coupling constants between the phosphorus atom and the vinyl protons. Moreover, the irradiation of **4** yielded a new type of β-diethoxyphosphinyl-α-alkene-α-imine, which later rearranged into the corresponding nitrile.

Although there have been fairly many reports on the synthesis and reaction of the saturated phosphinylalkane, only a little attention has been paid to the unsaturated phosphinyl derivative. We ourselves have reported the synthesis of β-diethoxyphosphinyl-α-alkene and ethyl β-diethoxyphosphinyl-α-alkenoate (**1**) by the reaction of α-nitro-α-alkene or ethyl α-nitro-α-alkenoate with triethyl phosphonate in one step.[2,3)]

Because of the pharmacological and structural interest of phosphinyl-2*H*-azirene, aziridine,[4-6)] or other phosphinyl derivatives,[7,8)] the replacement of the dibromo derivative of **1** (**2**) with sodium azide and the photochemical transformation of the azido derivatives thus obtained will be examined in this paper.

Results and Discussion

*Reaction of **2** with Sodium Azide.* The addition of bromine to 2-diethoxyphosphinyl-1-butene (**1a**), 2-diethoxyphosphinyl-3-methyl-1-butene (**1b**), and ethyl 3-diethoxyphosphinyl-2-pentenoate (**1c**) in chloroform at room temperature for a day gave the corresponding dibromo derivatives, 1,2-dibromo-2-diethoxyphosphinylbutane (**2a**), 1,2-dibromo-2-diethoxyphosphinyl-3-methylbutane (**2b**), and ethyl 2,3-dibromo-2-diethoxyphoshpinyl-pentanoate (**2c**), in good yields.

The ratio of the geometric isomers (*E*-isomer : *Z*-isomer=50 : 50) in **1**, as determined from the intensity of the olefinic proton signals, was maintained in the diastereomers (*erythro* : *threo*=50 : 50) in **2**.

Since the dehydrobromination of **2a**, **b** with triethylamine scarcely proceeded at, all a solution of **2a** in dimethylformamide was treated with sodium azide with stirring at 40—45 °C for 24—35 hr to give 1-bromo-2-diethoxyphosphinyl-1-butene (**3a**) as the main product, together with a small amount of 1-azido-2-diethoxyphosphinyl-2-butene (**5a**). The similar treatment of **2b** gave 1-azido-2-diethoxyphosphinyl-3-methyl-2-butene (**5b**) as the main product, along with a small amount of 1-bromo-2-diethoxyphosphinyl-3-methyl-2-butene (**3b**). Compound **3a** was also obtained in a good yield by the reaction of **2a** with liquid ammonia in a sealed tube at room temperature for 2 days. The treatment of **3a** or **3b** with sodium azide with stirring at 50—55 °C for 45—50 hr gave 1-azido-2-diethoxyphosphinyl-1-butene (**4a**) or 1-azido-2-diethoxyphosphinyl-3-methyl-1-butene (**4b**) respectively in a good yield. On the contrary, the dehydrobromination of **2c** proceeded smoothly with triethylamine to give ethyl 2-bromo-3-diethoxyphosphinyl-2-pentenoate (**3c**); ethyl 2-azido-3-diethoxyphosphinyl-2-pentenoate (**4c**) could not be obtained. This fact may be attributed to the inactivity of the α-bromo atom of the α, β-unsaturated carboxylic ethyl ester. Compounds **3**, **4** and **5** were separated by distillation under reduced pressure or by chromatography on a silica-gel column, using benzene–acetone as the eluent. It is interesting that **3**, **4** and **5** are all composed of only one geometric isomer. The yields, physical constants, and spectral data are summarized in Tables 1 and 2.

The stereochemical assignment of **3**, **4** and **5** was made on the basis of elementary and spectroscopic analyses. The IR spectra of **3** and **4** showed a weak band of the carbon-carbon double bond in the 1575—1618 and 1610 cm^{-1} regions respectively, and strong bands of the diethoxyphosphinyl group in the 1240—1260 (≫P=O) and 1020—1025 (≫P–O–C) cm^{-1} regions, while that of **5** showed a band of the carbon-carbon double bond at 1625—1630, ≫P=O in the 1235—1250 region, and ≫P–O–C at 1025 cm^{-1}. The absorption pattern of **3**, **4** and **5** is essentially the same as that of the starting material (**1**) except for the characteristic strong azido band of **4** and **5** appearing in the 2100—2110 cm^{-1} region. The NMR spectra of **3**, **4** and **5** showed a vinyl hydrogen signal in the α- or γ-position with regard to the β-phosphorus atom in lower magnetic fields, and with smaller coupling constants ($J_{P,H}$=12.0—23.0 Hz), in comparison with those of the *E*-isomer ($J_{P,H}$=22.3—23.0 Hz) and the *Z*-isomer ($J_{P,H}$=48.0—59.0 Hz) of **1**[3)] and others appearing in the literature.[9)] From the above results, it may be deduced that the dehydrobromination of **2** proceeded stereoselectively to give only an *E*-isomer and that the configuration was retained in the subsequent substitution of the bromine atom of **3** with the azido group.

*Irradiation of **4a** and **5b**.* A solution of **4a** in cyclohexane was irradiated in a stream of nitrogen by means of an external high-pressure mercury lamp for

Table 1. The yields, boiling points and elementary analyses of **2**, **3**, **4**, and **5**

Compound	Yield (%)	bp °C/mmHg	Formula	Found (Calcd), % C	H	N
2a	73.5	100—105/0.1	$C_8H_{17}O_3PBr_2$	27.18 (27.29	4.99 4.87)	
2b	70.5	105—109/0.42	$C_9H_{19}O_3PBr_2$	29.50 (29.53	5.67 5.23)	
2c	71.3	syrup[a]				
3a	61.6	67— 72/0.16	$C_8H_{16}O_3PBr$	35.13 (35.44	6.20 5.95)	
3b	9.2	65— 67/0.09	$C_9H_{18}O_3PBr$	37.95 (37.91	6.27 6.27)	
3c	30.0	syrup	$C_{10}H_{18}O_5PBr$	36.65 (36.49	5.90 5.51)	
4a	70.6	syrup	$C_8H_{16}N_3O_3P$	40.92 (41.20	7.15 6.92	18.40 18.02)
4b	62.5	syrup	$C_9H_{18}N_3O_3P$			17.23 (17.00)
5a	7.2	73— 77/0.25	$C_8H_{16}N_3O_3P$			18.34 (18.02)
5b	70.3	80— 85/0.25	$C_9H_{18}N_3O_3P$	43.75 (43.72	7.48 7.29	17.16 17.00)

a) Unstable syrup for distillation, the structure of which was confirmed by means of spectral data and the conversion into **3c**.

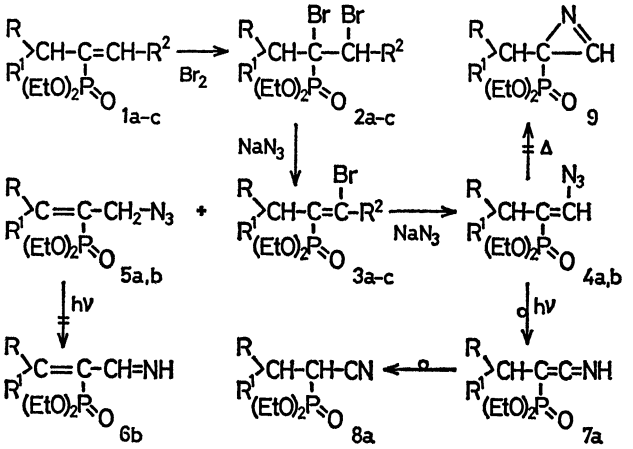
Table 2. Spectral data of **2**, **3**, **4**, and **5**

Compound	IR spectrum, cm^{-1} in KBr N_3(s)[a]	C=C(w)[b]	P=O(s)	P-O-C(s)	NMR spectrum, δ in $CDCl_3$ α-H (γ-H)	$J_{P,H}$(Hz)
2a			1250,	1020	3.75—4.10m[c]	
2b			1255,	1020	3.65—4.07m	
2c			1255,	1020	4.70—4.97m	
3a		1590,	1250,	1025	7.24d[d]	15.0
3b		1575,	1250,	1025	7.24d	15.0
3c		1618,	1260,	1020	(2.01d)	12.0
4a	2100,	1610,	1250,	1025	7.18d	14.0
4b	2100,	1595,	1240,	1025	7.28d	19.0
5a	2110,	1630,	1250,	1025	4.40d	23.0
5b	2110,	1625,	1235,	1025	4.95d	

a) s=Strong. b) w=Weak. c) m=Multiplet. d) d=Doublet.

a day until the azido band at *ca.* 2100 cm^{-1} had disappeared at room temperature; the chromatographic separation of the resultant solution gave 2-diethoxyphosphinyl-1-butene-1-imine (**7a**) in a 30% yield and a small amount of 2-diethoxyphosphinyl-butanenitrile (**8a**), instead of the expected 1-ethyl-1-diethoxyphosphinyl-2*H*-azirene (**9**). Since the irradiation of the isolated **7a** gave **8a** in a 17% yield, it was concluded that **8a** was derived from **7a** by the 1,3-shift of hydrogen.[10] On the other hand, the irradiation of **5b** in cyclohexane in a stream of nitrogen by means of a high-pressure mercury lamp gave several kinds of products, none yielding the expected 2-diethoxyphosphinyl-3-methyl-2-butene-1-imine (**6b**). The structures of the products are now under investigation.

The IR spectrum of **7a** showed a characteristic strong band at 2070, and that of **8a** showed a weak nitrile band at 2250 cm^{-1}, causing the band at



a; R=CH_3, R^1=R^2=H b; R=R^1=CH_3, R^2=H c; R=CH_3, R^1=H, R^2=COOEt

Scheme 1.

2070 cm^{-1} to disappear. On the other hand, the NMR spectrum of **7a** showed the imino proton signal at δ 4.80. These spectral data support the structures of **7** and **8**.

Experimental

All the boiling points are uncorrected. The IR spectra were recorded with a Hitachi EPI-S2 Spectrometer. The NMR spectra were measured with a JNM-4H-100 Spectrometer (Japan Electron Optics Laboratory Co., Ltd.), using tetramethylsilane as the internal standard.

Material. Compounds **1a**—**c** were prepared by the method previously reported.[3]

*Reaction of **1a** and **1b** with Bromine.* Into a solution of **1a** (19.2 g, 0.1 mol) in chloroform (70 ml), a solution of bromine (16 g, 0.1 mol) in chloroform (30 ml) was stirred portion by portion, at room temperature. The resultant solution was sealed tightly in a vessel (200 ml) and allowed to stand overnight at room temperature, and then the solution was concentrated. The residual oil was distilled under reduced pressure to give **2a** as a colorless oil.

In a similar manner, equimolar amounts of **1b** and bromine were reacted to give **2b** as a colorless oil after standing for 2 days.

*Reaction of **1c** with Bromine.* Into a solution of **1c** (7.5 g, 0.03 mol) in chloroform (30 ml), a solution of bromine (4.8 g, 0.03 mol) in chloroform (10 ml) was stirred at room temperature. After having been heated in a sealed tube at 100 °C for 12 hr, the reaction solution was concentrated. The residual syrup was purified on a silica-gel column, using benzene–acetone (10 : 1 V/V) as the eluent; the eluent solvent was then evaporated under reduced pressure to give **2c** as a colorless syrup which could not be distilled.

*Reaction of **2a** and **2b** with Sodium Azide.* Into a mixture of sodium azide (3.9 g, 0.06 mol) in dry dimethylformamide (50 ml), we stirred a solution of **2a** (7.04 g, 0.02 mol) in dimethylformamide (5 ml), portion by portion, at room temperature. After continuous stirring at 40 °C for 25 hr, the reaction solution was poured into ice water (300 ml), and then the aqueous solution was stirred for 1 hr. The solution was extracted well with benzene (100 ml) three times. The benzene extracts were washed with water twice, dried over anhydrous sodium sulfate, and then evaporated under reduced pressure to give a yellow oil. The purification of the oil on a silica-gel column, using benzene–ethyl ether (20 : 1 V/V) as the eluent, and the evaporation of the eluent solvent under reduced pressure gave **3a** from the first fraction and **5a** from the last fraction, both as colorless oils.

In a similar manner, Compound **2b** was reacted with sodium azide in dimethylformamide to give **3b** and **5b**.

*Reaction of **2a** with Liquid Ammonia.* Compound **2a** (7.04 g, 0.02 mol) was dissolved in liquid ammonia (15 ml), and then the solution was allowed to stand in a sealed tube at room temperature for 2 days. To the reaction solution, dry chloroform (20 ml) was then added. After the removal of the ammonium bromide deposited, the chloroform solution was concentrated. The residual oil was purified on a silica-gel column, using benzene–ethyl ether (20 : 1 V/V), to give **3a** as a colorless oil in a 67.5% yield.

*Reaction of **3a** and **3b** with Sodium Azide.* Into a mixture of sodium azide (6.5 g, 0.1 mol) in dry dimethylformamide (70 ml), a solution of **3a** (3.8 g, 0.014 mol) in dimethylformamide (5 ml) was stirred, portion by portion, at room temperature. After continuous stirring at 50 °C for 56 hr, the reaction solution was poured into ice water (300 ml), and then the aqueous solution was stirred for 1 hr. The solution was extracted well with benzene (100 ml) three times. The benzene extracts were washed with water twice, dried over anhydrous magnesium sulfate, and finally evaporated under reduced pressure to give a yellow syrup. Purification on a silica-gel column, using benzene–ethyl ether (10 : 1 V/V), and the evaporation of the eluent solvent under reduced pressure gave **4a** as a colorless syrup.

In a similar manner, Compound **4b** was obtained as a colorless syrup by the reaction of **3b** with sodium azide in dimethylformamide.

*Reaction of **2c** with Sodium Azide.* Into a mixture of sodium azide (3.9 g, 0.06 mol) in dry dimethylformamide (50 ml), we stirred, portion by portion, a solution of **2c** (8.2 g, 0.02 mol) in dimethylformamide (5 ml) at room temperature. After continuous stirring at room temperature for 15 hr, the reaction solution was poured into ice water (300 ml), and then the aqueous solution was stirred for 1 hr. The solution was extracted well with benzene (100 ml) three times. The benzene extracts were washed with water twice, dried over anhydrous magnesium sulfate, and then finally evaporated under reduced pressure to give a yellow syrup. The purification of the syrup on a silica-gel column, using benzene–acetone (7 : 1 V/V), and the evaporation of the eluent solvent under reduced pressure gave **3c** as a colorless syrup which could not be distilled.

*Irradiation of **4a**.* A solution of **4a** (2.0 g, 0.0086 mol) in cyclohexane (50 ml) was irradiated in a stream of nitrogen by means of a 500 W high-pressure mercury lamp at room temperature for 6 hr. After the removal of the solvent under reduced pressure, the residual syrup was purified on a silica-gel column, using carbon tetrachloride–acetone (5 : 1 V/V), and then the eluent solvent was evaporated to give **7a** in a 30% yield from the first fraction and **8a** in a 7% yield from the last fraction, both as colorless syrups. **7a**; IR (KBr disk): 2080 (C=C=N), 1635 (C=C), 1243 (P=O), and 1225 (P–O–C) cm^{-1}. NMR ($CDCl_3$): δ 4.80 (1H, broad s, NH) and 1.72—2.24 (2H, m, $CH_3\underline{CH_2}-\underset{|}{C}=$). The structure of **7a** was confirmed by means of the spectral data and by its conversion into **8a**. **8a**; IR (KBr disk): 2230 (C≡N), 1260 (P=O), and 1220 (P–O–C) cm^{-1}. NMR ($CDCl_3$): δ 2.70—3.14 (1H, m, $-CH_2\underline{\underset{|}{C}H}-C\equiv$).

Found: N, 6.58%. Calcd for $C_8H_{16}NO_3P$: N, 6.83%.

*Isomerization of **7a** to **8a**.* A solution of **7a** (0.2 g, 0.00086 mol) in dry tetrahydrofuran (30 ml) was irradiated in a stream of nitrogen by means of a 500 W high-pressure mercury lamp at room temperature for 10 hr. After the subsequent removal of the solvent under reduced pressure, the residual syrup was purified on a silica-gel column, using benzene–acetone (5 : 1 V/V), and then the solvent was evaporated under reduced pressure to give **8a** in a 17% yield.

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