BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 474—477 (1971)

The Reaction of α-Oxo Acids with *N*-Phenyltriphenylphosphinimine[1]

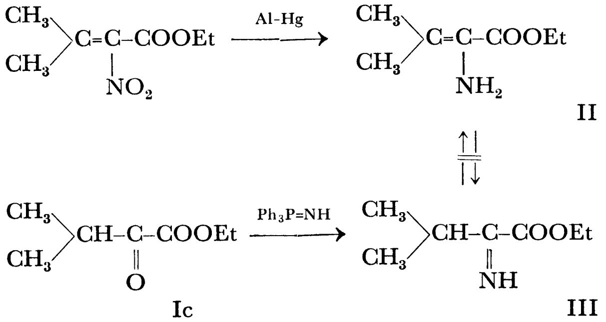
Chung-gi SHIN,* Hiroaki ANDO, and Juji YOSHIMURA

Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo

(Received May 25, 1970)

The reaction between ethyl α-oxocarboxylate and *N*-phenyltriphenylphosphinimine gave a mixture of ethyl α-phenyliminocarboxylate (IVa—f) and the tautomeric isomers (Va—f) in good yield. IVa and Va derived from ethyl pyruvate was converted gradually into 3-anilino-5-ethoxycarbonyl-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one (VIIa) on standing at room temperature. The free acid of IVa and Va prepared by the same method could not be purified, but a small amount of 3-anilino-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one (IX) was obtained from the reaction mixtures. In the reaction of aniline and pyruvic acid, α,γ-dianilino-γ-carboxy-α-methyl-γ-butyrolactone (XII) was obtained in the neutral reaction condition and 4-anilino-2-phenyliminopentanoic acid (XIV) in basic condition. The structure of the products was proved by NMR and IR spectrum, and the reaction courses were discussed.

In the previous paper, one of the authors reported the isolation of a primary enamine (ethyl α-amino-β-methylcrotonate (II)) by the reduction of the corresponding α,β-unsaturated α-nitrocarboxylic ester, and the tautomeric imine (ethyl 2-imino-3-methylbutanoate (III)) by the reaction of the corresponding α-oxocarboxylic ester (Ic) with triphenylphosphinimine (Scheme 1). The acylation of both II and III yielded the same enamine derivative,[2—4] and the isomerization between II and III was not reached.



Scheme 1

On the other hand, Wieland *et al.*[5] have reported that a treatment of pyruvic acid (Ia′) with aniline[6,7] did not yield any amount of α-phenyliminopropionic acid (IVa′). However, it was expected from our previous result that the reaction of *N*-phenyltriphenylphosphinimine with α-oxocarboxylic acids would give the homologue of IVa′ and/or the tautomeric isomers.

In the present paper, the reactions of α-oxocarboxylic acid (Ia′) or α-oxocarboxylic esters (Ia—f) with *N*-phenyltriphenylphosphinimine or aniline were described.

Results and Discussion

Ethyl pyruvate (Ia) was treated with *N*-phenyltriphenylphosphinimine[8] in anhydrous acetonitrile under reflux. Triphenylphosphine oxide precipitated quantitatively was removed by filtration and the filtrate was distilled under the reduced pressure to afford pale yellow oil in a 66% yield, which was a mixture of the corresponding imine (IVa) and enamine (Va) (Scheme 2). The infrared spectrum of the mixture of IVa and Va showed absorption bands at 3350 (NH), 1730—1720 (two COOEt), 1650 (C=N) and 1590 (C=C) cm^{-1}, while the NMR spectrum showed peaks at τ2.55—3.40 (m, two C_6H_5 and vinyl protons, *ca.* 10.9H), 5.62 (two q, $-CH_2-$, 4H), 7.58 (s, NH in Va, *ca.* 0.3H), 7.92 (s, $-\underset{\|}{C}-CH_3$ in IVa, *ca.* 2.2H), and 8.62 (two t, $-CH_3$ in IVa and Va, 6H). From the intensity of $-\underset{\|}{C}-CH_3$ proton signal of IVa and $-\underset{|}{C}{=}CH_2$ proton signal of Va, the yield was determined to be 47.4 and 18.6%, respectively. α-Oxocarboxylic esters (Ib—f), on being treated with *N*-phenyltriphenylphosphinimine, afforded similarly the corresponding mixtures (IVb—f and Vb—f). In other cases, these

---

[1] This paper was presented at the 22nd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1969.

* Present Address: Laboratory of Organic Chemistry, Faculty of Technology, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama. To whom inquires should be addressed.

[2] C. Shin, M. Masaki, and M. Ohta, This Bulletin, **39**, 858 (1966).

[3] C. Shin, M. Masaki, and M. Ohta, *J. Org. Chem.*, **32**, 1860 (1967).

[4] M. Masaki, C. Shin, H. Kurita, and M. Ohta, *Chem. Commun.*, **1968**, 1447.

[5] T. Wieland, G. Ohnacker, and R. K. Rothhaupt, *Chem. Ber.*, **88**, 633 (1955).

[6] L. Simon, *Ann. Chem.*, **188**, 336 (1877); *C. R. Acad. Sci., Paris*, **118**, 1342 (1894).

[7] C. Böttinger, *Ber.*, **10**, 818 (1877); *Ann. Chem.*, **188**, 366 (1877).

[8] R. Appel and A. Hauss, *Z. Anorg. Chem.*, **311**, 290 (1961).

TABLE 1. THE MIXTURES OF ETHYL α-PHENYLIMINO (IVa-f) AND α-ANILINO (Va-f) CARBOXYLATES

Compd. IV+V	R	R′	Bp °C/mmHg	Yield (%)	Formula	Found, % C	Found, % H	Found, % N	Calcd, % C	Calcd, % H	Calcd, % N
a	H	H	94—96/1	66	$C_{11}H_{13}NO_2$	69.28	6.93	7.51	69.09	6.85	7.33
b	H	CH_3	89—93/1.5	55	$C_{12}H_{15}NO_2$	70.37	7.07	6.43	70.22	7.37	6.82
c	CH_3	CH_3	91—94/2	53	$C_{13}H_{17}NO_2$	71.22	7.49	6.61	71.20	7.82	6.39
d	H	CH_2CH_3	98—101/1.5	66	$C_{13}H_{17}NO_2$	71.68	7.43	6.49	71.20	7.82	6.39
e	H	$CH_2CH_2CH_3$	100—101/1	53	$C_{14}H_{19}NO_2$	72.08	8.11	6.41	72.07	8.21	6.00
f	H	$CH(CH_3)_2$	106—109/2	52	$C_{14}H_{19}NO_2$	71.97	7.92	6.29	72.07	8.21	6.00

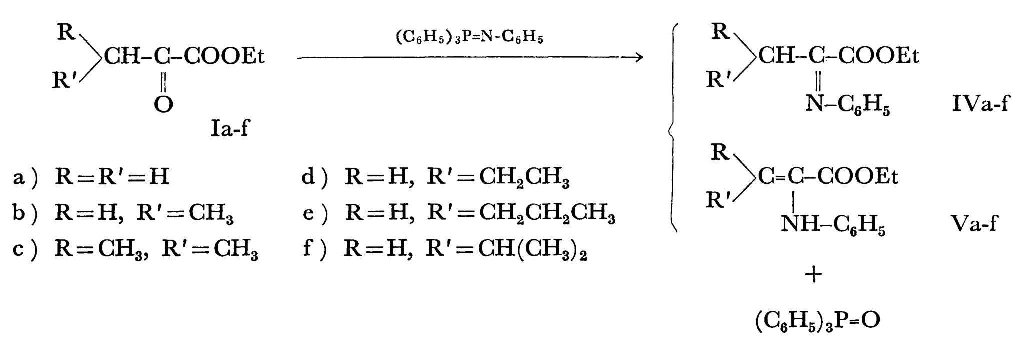
TABLE 2. THE IR SPECTRUM OF THE MIXTURE OF IVa-f AND Va-f

Compd. IV+V	R	R′	IR Spectrum (cm^{-1}, in NaCl) NH	COOEt		C=N	C=C
a	H	H	3350	1720	1730	1650	1590
b	H	CH_3	3400	1720	1730	1650	1590
c	CH_3	CH_3	3400	1720	1730	1660	1600
d	H	CH_2CH_3	3400	1720	1730	1650	1595
e	H	$CH_2CH_2CH_3$	3400	1720	1730	1650	1595
f	H	$CH(CH_3)_2$	3400	1730	1740	1650	1600

TABLE 3. THE NMR SPECTRUM OF THE MIXTURE OF IVa-f AND Va-f (τ-Value, in $CDCl_3$)

Compd. IV+V	R	R′	$\overset{R'}{\overset{\vert}{\text{R-C-}}}$	$\overset{R'}{\overset{\vert}{\text{R-C=}}}$	-NH-	Composition (%) IV[e)]	V[e)]
a	H	H	7.92 (s)	2.55—3.40[b)]	7.58 (s)	47.4	18.6[g)]
b	H	CH_3	7.40 (q)	3.58 (q)	4.55 (bs)[c)]	33	22[h)]
c	CH_3	CH_3	7.15 (sp)[a)]	—	5.79 (bs)[c)]	10.4	42.6[f,i)]
d	H	CH_2CH_3	7.45 (t)	3.73 (t)	4.32 (bs)[c)]	52.8	13.2[i)]
e	H	$CH_2CH_2CH_3$	7.29 (t)	3.65 (t)	2.30—3.50[b)]	23.3	28.7[j)]
f	H	$CH(CH_3)_2$	7.57 (d)	3.80 (d)	4.57 (s)[d)]	27.5	25.5[k)]

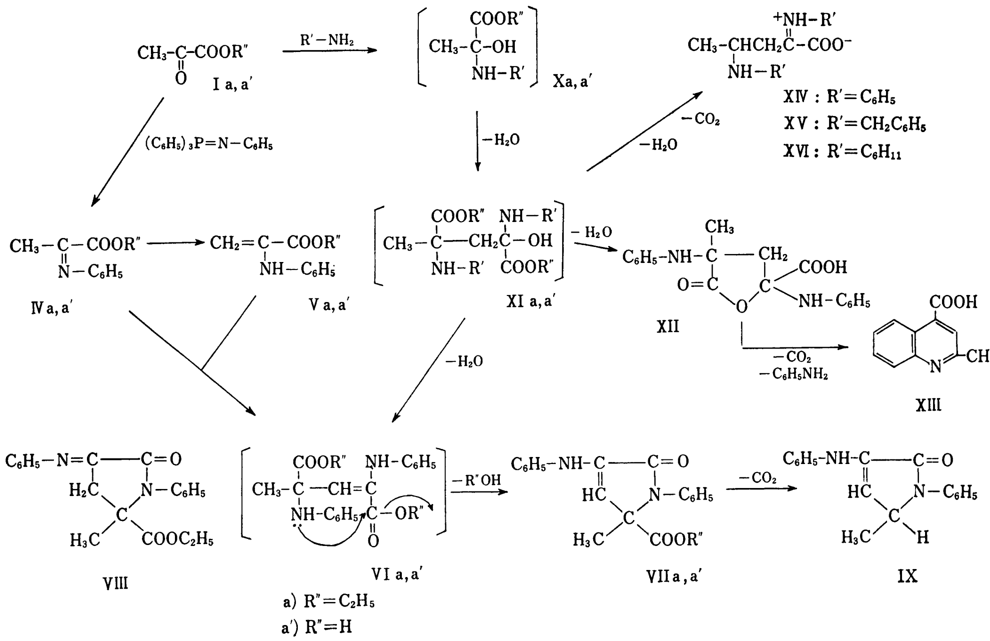
a) sp=Septet. b) Overlap in benzene ring protons. c) bs=Broad singlet. d) In CCl_4. e) Evaluated from the intensity of methylene and vinyl protons in the β-position of IV and V. f) Evaluated from the intensity of methylene protons in the β-position and NH proton. g) Standing for 3 days at 5°C. h) Standing for 1 day at room temperature. i) Standing for 3 days at room temperature. j) Standing for 5 days at 5°C. k) Redistilled after standing for 4 days at room temperature.



Scheme 2

ratios were evaluated from that of methylene and vinyl protons in the β-position of IV and V. The yields and some spectral data of the mixtures are summarized in Tables 1, 2 and 3.

On standing for a week at room temperature, the mixture (IVa and Va) became viscous and colored gradually, and then a part of the oil crystallized. This crystalline compound (VIIa) was identified as the same product obtained from Ia and aniline, and assigned as 5-ethoxycarbonyl-5-methyl-3-phenylimino-2-pyrrolidinone (VIII) by Simon.[9)] However, VIIa showed the peaks at τ2.55—3.09 (m, tow C_6H_5 and NH, 11H), 4.03 (s, vinyl proton, 1H), 5.85 (q, $\underline{CH_2}$-CH_3, 2H), 8.36 (s, CH_3, 3H) and 8.80 (t, $CH_2\underline{CH_3}$), while the infrared spectrum showed the absorption bands of NH at 3270, of ester at 1720, of carbonyl at



Scheme 3.

1680, and of carbon-carbon double bond at 1640 cm^{-1}. The presence of one vinyl proton, and NH and C=C absorption in the above data indicates that VIIa is 3-anilino-5-ethoxycarbonyl-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one, the enamine form of VIII. In order to explore the intermediate step for the formation of VIIa, the conversion of viscous and colored oil into VIIa was followed spectrometrically. The appearance of two NH (τ6.15, s) and new vinyl proton signal (τ5.15, s) indicates that the reaction of IVa and Va proceeds through the formation of ethyl 2,4-dianilino-4-ethoxycarbonyl-2-pentenoate (VIa).

Simon has reported the treatment of Ia' with aniline in ether gave a small amount of 4-anilino-2-phenyliminopentanoic acid (XIV) and α,γ-dianilino-γ-carboxy-α-methyl-γ-butyrolactone (XII),[9] which was converted into 4-carboxy-2-methylquinoline (XIII).[6] This reaction was reinvestigated in detail under various condition. The treatment of Ia' with amines (aniline, benzylamine and cyclohexylamine) in the presence of triethylamine gave 4-(substituted-amino)-2-(substituted-imino)pentanoic acids (XIV—XVI), while in the absence of triethylamine the treatment of Ia' with aniline afforded XII, which was qantitatively converted into XIII by heating in water, accompanying with the liberation of CO$_2$ and aniline. It was assumed that an intermediate (XIa') formed *via* α-hydroxy-α-alkylaminopropionic acid (Xa') was subjected to decarboxylation, β-elimination and isomerization in a basic media to give XIV—XVI, but in neutral condition XIa' yielded XII by intramolecular dehydration. The infrared spectrum of XIV—XVI showed the absorption bands of NH (3250—3273), carbon-nitrogen double bond (1620—1625) and carboxylate group (-COO$^-$) (1520—1540 cm^{-1}), and the structures of XIV—XVI were assigned on the basis of these spectral data.

In order to obtain IVa' and Va', the mixture of IVa and Va was hydrolysed with 10% potassium hydroxide at room temperature, but pyruvic acid (Ia') was obtained. Ia' was treated with *N*-phenyltriphenylphosphinimine to give a viscous syrup (IVa' and Va') in a good yield and triphenylphosphine oxide in almost quantitative yield. Attempts to purify the resultant syrup were unsuccessful. The crude syrup was esterified, which, on being allowed to stand for few weeks at room temperature, gave a small amount of VIIa. This fact indicates that IVa' and Va' are certainly formed by reaction of Ia' with *N*-phenyltriphenylphosphinimine. Moreover, the above assumption was supported by the fact that 3-anilino-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one (IX) is gradually precipitated from the mixture of IVa' and Va' in 50% ethanol on standing for 2 days at room temperature.

Experimental

All boiling and melting points are uncorrected. The IR spectrum was recorded with a Hitachi EPI-S2 Spectrometer. The NMR spectrum was measured with a JNM-4H-100 Spectrometer (Japan Electron Optics Laboratory Co., Ltd.) at 100 MHz.

Materials. *N*-Phenyltriphenylphosphinimine was prepared by the reaction of triphenylphosphine dibromide with aniline in the presence of triethylamine by the method reported.[10] Mp 126—128°C (lit, mp 128—130°C). The acetonitrile used was distilled from phosphorous pentoxide and dried over calcium hydride.

Reaction of Ethyl α-Oxocarboxylate with N-*Phenyltriphenylphosphinimine.* To a solution of ethyl α-oxocarboxylate (0.02 mol) in anhydrous acetonitrile (30 m*l*), *N*-phenyltriphenylphosphinimine (0.02 mol) was added and then the mixture was refluxed for 1 hr. On concentrating the resulting solution, a brown syrup remained, to which dry ether (30 m*l*)

---

9) L. Simon, *C. R. Acad. Sci., Paris*, **134**, 1063 (1902); *ibid.*, **144**, 140 (1907); *ibid.*, **147**, 126 (1908).

10) L. Hornor and H. Oediger, *Ann. Chem.*, **627**, 142 (1959).

Table 4. Physical constants of XIV-XVI

Compd.	R'	Mp °C	Yield (%)	Formula	Elemental analysis (%)				IR Spectrum (cm^{-1}, in KBr)		
						C	H	N	NH	C=N+	COO$^-$
XIV	C_6H_5	195—197[a,c]	70	$C_{17}H_{18}N_2O_2$	Found	72.36	6.68	9.91	3273	1620	1540
					Calcd	72.32	6.43	9.92			
XV	$CH_2C_6H_5$	205—208[b,c]	46	$C_{19}H_{22}N_2O_2$	Found	73.51	7.02	9.91	3270	1620	1520
					Calcd	73.52	7.14	9.03			
XVI	C_6H_{11}	260>[a,c]	60	$C_{17}H_{30}N_2O_2$	Found	69.19	9.73	9.92	3250	1625	1520
					Calcd	69.37	10.27	9.54			

a) Recrystallized from methanol. b) Recrystallized from ethanol. c) Colorless needles.

was added, and then triphenylphosphine oxide precipitated was filtered off. The ethereal solution was concentrated to one third of its volume and then allowed to stand overnight in a refrigerator. The further triphenylphosphine oxide precipitated was filtered off. After concentrating the ethereal solution, dry petroleum ether (20 m*l*) was added to the residual syrup and the small amount of triphenylphosphine oxide was filtered off, and then finally the solvent was removed by evaporation. Distillation of the resulting syrup afforded a pale yellow oil. The results are summarized in Tables 1, 2 and 3.

Confirmation of Ethyl 2,4-Dianilino-4-ethoxycarbonyl-2-pentenoate (VIa) as Intermediate. When the mixture of IVa and Va, or the reaction mixture of ethyl pyruvate (Ia) with aniline, was allowed to stand for few days at room temperature, the oil became colored and viscous gradually. This syrup was subjected to the measurements of IR abosrption in NaCl and of NMR absorption in $CDCl_3$ using tetramethylsilane as an internal standard. The results are described in the former section.

3-Anilino-5-ethoxycarbonyl-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one (VIIa). A) From Mixture of IVa and Va: When the above intermediate (VIa, 1 g) was allowed to stand for several days, the viscous syrup crystallized gradually. To the resulting product, a small quantity of dry ether was added, and then crystals precipitated were collected on a filter. Recrystallization from ethanol gave colorless prisms (0.5 g, 32%), mp 146—147°C.

Found: C, 71.62; H, 6.28; N, 8.29%. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33%.

B) From Ia and Aniline: A mixture of Ia (1.16 g) and aniline (0.93 g) was allowed to stand at room temperature for 3 days, during which water separated gradually in the reaction mixture, and crystalline product was obtained from the dark brown syrup. Recrystallization from petroleum ether (bp 70—120°C) gave colorless prismatic needles (0.62 g, 37%), mp 144—146°C. The melting point of this compound was not depressed on admixture with the compound obtained from procedure *A*.

Reaction of Pyruvic Acid and Amines (Aniline, Benzylamine, and Cyclohexylamine) in the Presence of Triethylamine. To a solution of pyruvic acid (0.025 mol) in dry ether (25 m*l*) with the presence of triethylamine (0.025 mol), amine (0.025 mol) was added drop by drop with stirring below 5°C. After standing for 2 hr in a refrigerator, the reaction mixture was kept overnight at room temperature. A red syrup in the bottom crystallized upon addition of water. Recrystallization from methanol or ethanol afforded colorless needles. results are summarized in Table 4.

Reaction of Pyruvic Acid and N*-Phenyltriphenylphosphinimine. A) Esterification of the Reaction Product:* To a solution of pyruvic acid (1.1 g) in dry acetonitrile (40 m*l*), *N*-phenyltriphenylphosphinimine (4.5 g) was added and then the mixture was refluxed for 1 hr. Triphenylphosphine oxide was removed out of the reaction mixture by the similar way to that for the reaction of ethyl α-oxocarboxylate. Thus obtained syrup was dissolved in ethanol (50 m*l*) and heated under reflux for 3 hr in the presence of *p*-toluenesulfonic acid (0.5 g) and concentrated sulfuric acid (0.5 m*l*). The solution was concentrated under a reduced pressure to give residual oil, which was extracted with ether. The ethereal extract was washed with water and dried over anhydrous sodium sulfate and then the solvent was evaporated. This oil, without further purification, was allowed to stand for few weeks at room temperature to yield a small amount of crystals. This compound was the same as VIIa. Yield 0.08 g.

B) 3-Anilino-5-methyl-1-phenyl-Δ^3-pyrrolin-2-one (IX). In the above procedure *A*), the final syrup (4.8 g) after removal of triphenylphosphine oxide was diluted with 50% ethanol (50 m*l*). On standing for 2 days at room temperature, crystals precipitated. Recrystallization from ethanol gave pale yellow needles (1.1 g), mp 175—178°C. IR (KBr): 3350 (νNH), 1680 (νC=O) and 1660 (νC=C) cm^{-1}. NMR ($CDCl_3$): 3.44 (broad s, NH, 1H), 3.95 (d, vinyl proton, 1H), 5.74 (double q, methine proton, 1H), and 8.74 (d, methyl protons, 3H)τ.

Found: C, 77.23; H, 6.27; N, 10.43%. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60%.

The authors are indebted to Mr. Kiyofumi Fukukawa of our Laboratory for the NMR measurement.