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Syntheses and Reactions of *N*-(Phenylpyruvoyl) Amino Acids

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α-Ethoxy- and α-acetoxycinnamoyl chlorides were synthesized by treatments of α-ethoxy- and α-acetoxycinnamic acid with thionyl chloride and oxalyl chloride, respectively, and reactions of amino acid esters with the cinnamoyl chlorides were investigated in order to seek for a synthetic method of *N*-(phenylpyruvoyl) amino acids. *N*-Hydroxy- or *N*-benzyloxy-DL-alanine esters prepared from 2-bromopropionic esters and hydroxylamine or benzyloxyamine were treated with α-ethoxycinnamoyl chloride to give the corresponding *N*-(α-ethoxycinnamoyl) derivatives. Treatment of L-leucine ethyl ester with α-acetoxycinnamoyl chloride afforded *N*-(α-acetoxycinnamoyl)-L-leucine ethyl ester, the removal of the acetyl group from which was readily accomplished under mild, basic conditions, and *N*-(phenylpyruvoyl)-L-leucine ester was obtained. Treatment of the ester with ammonia yielded 3-benzylidene-6-isobutyl-2,5-piperazinedione.

There have been known several synthetic routes to *N*-pyruvoyl amino acids. Bergmann and his coworkers reported the formation of *N*-pyruvoylglycine or *N*-pyruvoylalanine on the acid hydrolysis of 3-methylene-2,5-piperazinediones prepared from *N*-glycyl- or *N*-alanylserine.[1] They have also described that some *N*-pyruvoyl or *N*-(phenylpyruvoyl) amino acids were prepared by the reaction of 4-acetamido-2,4-dimethyl- or 4-benzylidene-2-methyl-5-oxazolone with amino acids followed by acid hydrolysis of the resultant 2,2-diacetamidopropionyl[2] or α-acetamidocinnamoyl amino acids.[3] Direct condensations of pyruvic acid with amino acid esters by means of dicyclohexylcarbodiimide or phosphorus oxychloride have been reported by Stoll *et al.*[4] and Wieland *et al.*[5]

In our approach to the synthesis of *N*-(phenylpyruvoyl) α-hydroxyamino acids, the coupling methods of phenylpyruvic acid and α-hydroxyamino acids were studied. This paper deals with the preparation of α-ethoxy- and α-acetoxycinnamoyl chlorides and those reactions with α-amino and α-hydroxyamino acids.

α-Hydroxyamino acids have been reported to be prepared by the reaction of α-halo acids with hydroxylamine,[6] the hydrolysis of α-hydroxyamino nitriles,[7] or the hydrolysis of nitrones.[8] *N*-Hydroxy-DL-alanine *t*-butyl ester (Ia) was prepared in 98% yield by heating *t*-butyl 2-bromopropionate with hydroxylamine in methanol in the presence of triethylamine for 20 hr. Analogously, *N*-benzyloxy-DL-alanine *t*-butyl ester (Ib) and *N*-benzyloxy-DL-alanine ethyl ester (Ic) were readily prepared by condensations of the esters of 2-bromopropionic acid with benzyloxyamine in acetonitrile in 42% and 59% yield, respectively.

Some attempted reactions of 4-benzylidene-2-methyl-5-oxazolone with *N*-benzyloxy-DL-alanine ethyl ester (Ic) failed to give the *N*-(α-acetoamidocinnamoyl) derivative of the latter, but led only to recovery of the starting materials, possibly owing to the weakness of the nucleophilicity of the amine (Ic). The acid chloride method was then adopted for the coupling reaction. In order to protect the ketonic group of phenylpyruvic acid for such a reaction, the enol ether and the enol ester were employed.

α-Ethoxycinnamic acid was treated with thionyl chloride to give α-ethoxycinnamoyl chloride (II) in 92% yield, which was characterized by conversion to the corresponding anilide. Treatment of L-leucine ethyl ester (III) with the chloride (II) gave *N*-(α-ethoxycinnamoyl)-L-leucine ethyl ester (V), which was characterized by its conversion to the corresponding acid or amide. The hydrolysis of the enol ester moiety was attempted by treating with glacial acetic acid-hydrochloric acid, but the

1) a) M. Bergmann, A. Miekeley, F. Weinmann and E. Kann, *Heppe-Seyler's Z. physiol. Chem.*, **143**, 108 (1925); b) M. Bergmann, A. Miekeley and E. Kann, *ibid.*, **146**, 247 (1925).

2) M. Bergmann and K. Grafe, *ibid.*, **189**, 196 (1930).

3) J. S. Fruton and M. Bergmann, *J. Biol. Chem.*, **166**, 449 (1946).

4) A. Stoll, A. Hofmann, H. G. Leemann, H. Ott and H. R. Schenk, *Helv. Chim. Acta*, **39**, 1165 (1956).

5) T. Wieland, B. Heinke and K. H. Shin, *Chem. Ber.*, **91**, 483 (1958).

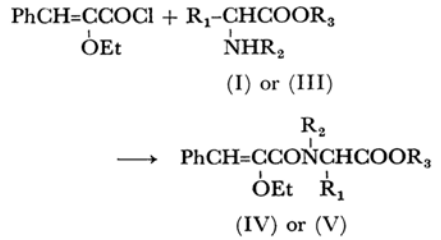
6) A. H. Cook and C. A. Slater, *J. Chem. Soc.*, **1956**, 4130.

7) a) W. Traube, *Ber.*, **27**, 1507 (1894); b) L. Neelakantan and W. H. Hartung, *J. Org. Chem.*, **23**, 964 (1958).

8) E. Buehler and G. B. Brown, *ibid.*, **32**, 265 (1967).

starting material was recovered.

Acylation of *N*-hydroxy-DL-alanine *t*-butyl ester (Ia) with the chloride (II) yielded *N*-(*α*-ethoxycinnamoyl)-*N*-hydroxy-DL-alanine *t*-butyl ester (IVa) which gives a positive ferric chloride reaction characteristic of hydroxamic acid. The product IVa was confirmed by elemental analysis and the infrared spectrum. Analogously, treatment of *N*-benzyloxy-DL-alanine *t*-butyl ester (Ib) with the chloride (II) afforded *N*-benzyloxy-*N*-(*α*-ethoxycinnamoyl)-DL-alanine *t*-butyl ester (IVb) as an oily product in 69% yield, which was characterized by the infrared spectrum. When the ester IVb was treated with trifluoroacetic acid at room temperature for a day, both *t*-butyl and ethyl groups were removed and *N*-benzyloxy-*N*-(phenylpyruvoyl)-DL-alanine (VI) was obtained in 25% yield. Treatment of *N*-benzyloxy-DL-alanine ethyl ester (Ic) with the chloride (II) afforded *N*-benzyloxy-*N*-(*α*-ethoxycinnamoyl)-DL-alanine ethyl ester (IVc) as an oily product. Hydrolysis of the ester (IVc) with 20% aqueous sodium hydroxide failed to give the corresponding acid but furnished *α*-ethoxycinnamic amide (VII).[9] The catalytic hydrogenation of IVc gave *N*-(2-ethoxy-3-phenylpropionyl)-*N*-hydroxy-DL-alanine ethyl ester (VIII).



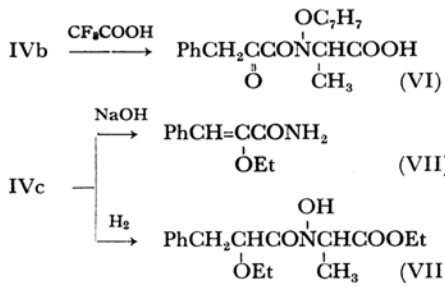
(I) or (III)

(IV) or (V)

I and IV
- a $R_1=CH_3$, $R_2=OH$, $R_3=t$-Bu
- b $R_1=CH_3$, $R_2=OC_7H_7$, $R_3=t$-Bu
- c $R_1=CH_3$, $R_2=OC_7H_7$, $R_3=Et$

III and V

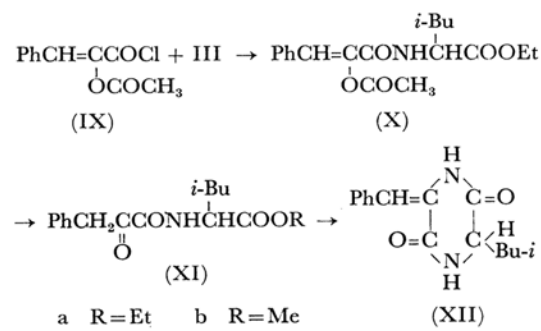
$R_1=i$-Bu, $R_2=H$, $R_3=Et$



(VI) (VII) (VIII)

α-Acetoxycinnamoyl chloride (IX) was synthesized in 79% yield by treating *α*-acetoxycinnamic acid with oxalyl chloride. The chloride was characterized by conversion into the corresponding anilide. Acylation of L-leucine ethyl ester (III) with the chloride (IX) afforded *N*-(*α*-acetoxycinnamoyl)-L-leucine ethyl ester (X) in 82% yield. The acetyl group was readily removed by treatment with aqueous sodium bicarbonate or with one equivalent of piperidine, and *N*-(phenylpyruvoyl)-L-leucine ethyl ester (XIa) was obtained in a good yield. The ester (XIa) was characterized by conversion to the 2,4-dinitrophenylhydrazone.

When the ester (XIa) was treated with ammonia in methanol, 3-benzylidene-6-isobutyl-2,5-piperazinedione (XII) was formed in 24% yield. The piperazinedione (XII) was directly obtained by treatment of X with ammonia in methanol. *N*-(Phenylpyruvoyl)-L-leucine prepared by the method of Bergmann *et al.*[3] was heated in methanol in the presence of hydrogen chloride to give the methyl ester (XIb), which, upon treatment with ammonia, also afforded the piperazinedione (XII).



(IX) (X) (XI) (XII)

a R=Et b R=Me

α-Acetoxycinnamoyl chloride appears to be the most convenient reagent for the synthesis of *N*-(phenylpyruvoyl) amino acids since the coupling reaction with amines and the removal of the protecting group are accomplished under milder conditions than those used in the aforementioned conventional method.

Experimental[10]

***N*-Hydroxy-DL-alanine *t*-Butyl Ester (Ia).** A solution of hydroxylamine prepared from the hydrochloride (7 g) and sodium (2.3 g) in methanol (90 m*l*) was added to a solution of *t*-butyl 2-bromopropionate (21.0 g) and triethylamine (10.1 g) in methanol (30 m*l*). The resultant solution was refluxed for 20 hr and then concentrated. Ether was added to the residue, and the insoluble substance, triethylamine hydrobromide (18 g), was filtered off. Evaporation of the ether afforded a crystalline residue which was treated with petroleum ether (bp 30—60°C) and collected. Yield was 16.0 g (98%). The product was recrystallized

9) The probable mechanisms for the reaction will be discussed in a subsequent paper.

10) All melting points were determined in a liquid bath and those and all boiling points are uncorrected. All concentrations and evaporations were carried out under reduced pressure. Infrared spectra were determined on a Hitachi EPI-S2 spectrophotometer as thin films of liquids, unless otherwise indicated. NMR spectra were recorded on JUM4H-100 spectrometer (Japan Electron Optics Laboratory Co.).

from petroleum ether (bp 50—90°C) to give colorless needles, mp 72.5—73.5°C.

Found: C, 52.05; H, 9.23; N, 8.34%. Calcd for $C_7H_{15}NO_3$: C, 52.15; H, 9.38; N, 8.69%.

IR (KBr): 3350 (OH), 3200 (NH), 1750 (COOBu-*t*) and 1170 cm^{-1}.

NMR ($CDCl_3$): τ 8.8 (d, 3H), 8.5 (s, 9H), 6.4 (q, 1H) and 3.5 (s, 2H).

***N*-Benzyloxy-DL-alanine *t*-Butyl Ester (Ib).** To a solution of *t*-butyl 2-bromopropionate[11] (10.0 g) in acetonitrile (100 m*l*) were added triethylamine (5.0 g) and benzyloxyamine[12] (6.0 g), and the solution was refluxed for 20 hr. After cooling, the resultant colorless needles (6.0 g) were filtered off. The filtrate was concentrated and the residue was dissolved in a mixture of ether and water. The ethereal layer was washed twice with water and dried over anhydrous sodium sulfate. After removal of the ether, the colorless oily residue was distilled to give a colorless oil (5.0 g, 42%), bp 126—127°C/2 mmHg.

Found: C, 67.15; H, 8.41; N, 5.53%. Calcd for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57%.

IR: 3240 (NH), 1730 (COOBu-*t*), 1370, 1225, 1160 and 700 cm^{-1}.

***N*-Benzyloxy-DL-alanine Ethyl Ester (Ic).** The procedure is essentially the same as for Ib. The product was obtained in 59% yield, bp 123—125°C/3.5 mmHg.

Found: C, 64.84; H, 7.52; N, 6.42%. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.68; N, 6.27%.

IR: 3250 (NH), 1730 (COOEt), 1320, 1180, 1020 and 700 cm^{-1}.

NMR (CCl_4): τ 8.9 (d, 3H), 8.8 (t, 3H), 6.45 (q, 1H), 5.85 (q, 2H), 5.4 (s, 2H) and 2.7 (s, 5H).

***α*-Ethoxycinnamoyl Chloride (II).** A mixture of α-ethoxycinnamic acid[13] (8.5 g) and thionyl chloride (18 m*l*) was refluxed for 30 min to afford a yellow clear solution. The excess thionyl chloride was evaporated and the residual oil was distilled to give a dark orange oil (8.6 g, 92%), bp 109°C/4 mmHg.

***α*-Ethoxycinnamic Anilide.** A solution of II (1 g) in ether (10 m*l*) was added to a solution of aniline (0.4 g) and pyridine (0.35 g) in ether (10 m*l*). The mixture was treated with water and the insoluble crystalline product was collected. Recrystallization of the product from carbon tetrachloride gave colorless needles (1.1 g, 85%), mp 125°C.

Found: C, 76.03; H, 6.56; N, 5.24%. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24%.

***α*-Ethoxycinnamic Amide (VII).** A solution of II (0.5 g) in ether was saturated with gaseous ammonia under ice cooling and allowed to stand for 2 hr at room temperature. The mixture was treated with water and the crystalline precipitates were collected and recrystallized from benzene to give colorless needles (0.3 g, 66%), mp 144°C.

Found: C, 69.30; H, 6.97; N, 7.62%. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33%.

IR (KBr): 3300, 3150 (NH_2), 1670 (C=C), 1620 (CONH), 1410, 1100, 1025 and 690 cm^{-1}.

***N*-(*α*-Ethoxycinnamoyl)-L-leucine Ethyl Ester (V).** A solution of II (1.5 g) in absolute ether (10 m*l*) was added portionwise, with stirring at 0°C, to a solution of L-leucine ethyl ester (1 g) and pyridine (0.6 g) in absolute ether (10 m*l*). After stirred at room temperature for additional 2 hr, the mixture was treated with water. The ethereal layer was washed successively twice with water, aqueous sodium bicarbonate, water, 1 N hydrochloric acid and finally twice with water, and dried over anhydrous sodium carbonate. Evaporation of the ether afforded a pale yellow oil (1.5 g, 63%), which was used without further purification.

IR: 3300 (NH), 1735 (COOEt), 1670 (C=C), 1635 (CONH) and 1515 (CONH) cm^{-1}.

***N*-(*α*-Ethoxycinnamoyl)-L-leucine.** A mixture of V (1 g) and 20% aqueous sodium hydroxide (10 m*l*) was stirred for 2 hr and water was added to the mixture until it became to a solution. Next day the aqueous solution was acidified with 3 N hydrochloric acid to afford a viscous oil. The oil was allowed to stand for 3 days in a refrigerator, when it had crystallized. Recrystallization from ligroin gave colorless needles (0.3 g, 33%), mp 101—102°C.

Found: C, 66.97; H, 7.51; N, 4.81%. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59%.

***N*-(*α*-Ethoxycinnamoyl)-L-leucine Amide.** A solution of V (1 g) in methanol (40 m*l*) was saturated with gaseous ammonia. The solution was heated at 70°C in the presence of ammonium chloride (0.3 g) in a sealed tube for 2 days and concentrated to dryness. The residue was dissolved in a mixture of ether and water, and the ethereal layer was washed twice with water and dried over anhydrous sodium sulfate. Removal of the ether gave a yellow oil which gradually crystallized. Recrystallization from carbon tetrachloride afforded colorless needles (0.3 g, 32%), mp 114.5—115.5°C.

Found: N, 9.47%. Calcd for $C_{17}H_{24}N_2O_3$: N, 9.20%.

***N*-Benzyloxy-*N*-(*α*-ethoxycinnamoyl)-DL-alanine *t*-Butyl Ester (IVb).** The procedure is essentially the same as for V. The product was obtained as a yellow oil in 69% yield, which was used without further purification.

IR: 2950, 1740 (COOBu-t), 1670 (C=C), 1660 (CON<), 1160 and 700 cm^{-1}.

***N*-Benzyloxy-*N*-(*α*-ethoxycinnamoyl)-DL-alanine Ethyl Ester (IVc).** The procedure is essentially the same as for V. The product was obtained as a yellow oil in 63% yield, which was used without further purification.

IR: 2950, 1740 (COOEt), 1660 (broad, C=C and CON<), 1210 and 700 cm^{-1}.

NMR (CCl_4): τ 8.8 (t, 3H), 8.7 (d, 3H), 8.5 (t, 3H), 6.0 (q, 2H), 5.9 (q, 2H), 5.15 (m, 1H), 5.05 (s, 2H), 3.9 (S, 1H), 2.8 (s, 5H) and 2.6 (m, 5H).

***N*-(*α*-Ethoxycinnamoyl)-*N*-hydroxy-DL-alanine *t*-Butyl Ester (IVa).** A solution of II (4.2 g) in absolute ether (30 m*l*) was added portionwise, with stirring, to a solution of Ia (3.2 g) and pyridine (1.6 g) in absolute ether (20 m*l*). After a day, the precipitated pyridine hydrochloride (1.9 g) was filtered off and the ethereal filtrate was washed twice with water and dried over anhydrous sodium sulfate. Evaporation of the ether afforded a pale yellow oil, which crystallized upon being allowed to stand in a refrigerator. Recrystallization from *n*-hexane gave pale yellow needles (3.4 g, 51%), mp 107—108°C. The product gave a wine red color with a methanolic ferric chloride solution.

11) A. Vollmar and M. S. Dunn, *J. Org. Chem.*, **25**, 387 (1960).

12) M. Masaki and M. Ohta, *ibid.*, **29**, 3165 (1964).

13) T. Gröger and E. Waldmann, *Monatsh. Chem.*, **89**, 370 (1958).

Found: C, 64.54; H, 7.62; N, 4.18%. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18%.

IR (KBr): 3300 (OH), 1740 (COOBu-*t*), 1660 (C=C), 1620 (CON<), 1450, 1160 and 690 cm^{-1}.

***N*-Benzyloxy-*N*-(phenylpyruvoyl)-DL-alanine (VI).** The crude IVb (1.0 g) was dissolved in trifluoroacetic acid (3 m*l*) and allowed to stand at room temperature for a day. Removal of the trifluoroacetic acid gave a pale black oil. The oil was dissolved in 1 N aqueous sodium hydroxide, and the solution was washed with ether, treated with activated charcoal and then acidified with 3 N hydrochloric acid. The precipitated oil was extracted with ether and the ethereal extract was dried over anhydrous sodium sulfate. Evaporation of the ether afforded the product as a yellow oil which was treated with petroleum ether (bp 30—60°C), thereby it crystallized gradually. The crystalline product (0.2 g, 25%) was collected and recrystallized from carbon tetrachloride into colorless powder, mp 107—108°C.

Found: C, 66.71; H, 5.54; N, 4.02%. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10%.

IR (KBr): 1750 (C=O), 1720 (COOH), 1630 (CON<), 1200 and 700 cm^{-1}.

NMR ($CDCl_3$): τ 8.5 (d, 3H), 6.0 (s, 2H), 5.15 (s, 2H) and 2.8 (s, 10H).

Reaction of IVc with Sodium Hydroxide. A mixture of IVc (1.0 g) and 20% aqueous sodium hydroxide (10 m*l*) was stirred at room temperature for 2 hr, and water was added to the mixture until it became to a solution. After a day, the aqueous solution was poured on water to afford α-ethoxycinnamic amide (VII) as crystalline precipitates (0.3 g, 62%). Recrystallization from carbon tetrachloride gave colorless needles which was identical, in melting point and infrared spectrum, with the sample obtained from the reaction of II with ammonia, mp 144°C.

***N*-(2-Ethoxy-3-phenylpropionyl)-*N*-hydroxy-DL-alanine Ethyl Ester (VIII).** The crude IVc (1 g) was reduced with hydrogen-5% palladium on charcoal (0.5 g) at 50 kg/cm^2 initial pressure in methanol (50 m*l*). After hydrogen absorption had ceased, the catalyst was removed and the solution was concentrated. A solution of the residue in ethyl acetate was treated with activated charcoal and reprecipitated by the addition of petroleum ether (bp 30—60°C). The product (0.2 g, 26%) was recrystallized from carbon tetrachloride to give colorless needles, mp 121.5—122.0°C.

Found: C, 62.30; H, 7.69; N, 4.62%. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53%.

IR (KBr): 3400 (OH), 1740 (COOEt), 1630 (CON<), 1220, 1190 and 705 cm^{-1}.

α-Acetoxycinnamic Acid. The procedure was modified from the method of Hemmerlé.[14] A suspension of phenylpyruvic acid (2 g) in acetic anhydride (5 m*l*) was refluxed for 2 hr in the presence of *p*-toluenesulfonic acid (0.1 g). On cooling, the resultant clear solution afforded colorless needles (2.0 g, 79%) which was collected and recrystallized from ethyl acetate to give colorless needles, mp 170.5—171.5°C (lit. 168°C,[14] 171—173°C[15]).

α-Acetoxycinnamoyl Chloride (IX). A suspension of the acid (2.0 g) in oxalyl chloride (5 m*l*) was refluxed for 2 hr. The resultant clear solution was concentrated and distilled to give a yellow oil (2.0 g, 92%), bp 105°C/0.07 mmHg.

Found: C, 59.05; H, 4.27%. Calcd for $C_{11}H_9O_3Cl$: C, 58.81; H, 4.04%.

α-Acetoxycinnamic Anilide. The procedure was essentially the same as for α-ethoxycinnamic anilide. Colorless needles from ethyl acetate, mp 171—172°C.

Found: C, 72.35; H, 5.38; N, 5.09%. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98%.

***N*-(α-Acetoxycinnamoyl)-L-leucine Ethyl Ester (X).** A solution of IX (3.7 g) in absolute ether (20 m*l*) was added portionwise with stirring to a solution of L-leucine ethyl ester (III) (2.6 g) and pyridine (1.14 g) in absolute ether (20 m*l*), and the mixture was stirred for 4 hr. The precipitated pyridine hydrochloride was filtered off and the ethereal filtrate was washed successively with water, aqueous sodium bicarbonate, water, 1 N hydrochloric acid and finally twice with water, and dried over anhydrous sodium sulfate. Evaporation of the ether afforded a crystalline residue which was recrystallized from *n*-hexane to give the product (4.7 g, 82%) as colorless scales, mp 94—96°C.

Found: C, 65.43; H, 7.21; N, 4.27%. Calcd for $C_{19}H_{25}NO_5$: C, 65.69; H, 7.25; N, 4.03%.

IR (KBr): 3320 (NH), 1755 (CH_3COO), 1730 (shoulder, COOEt), 1670 (C=C), 1640 (CONH), 1515, 1185, 1150 and 690 cm^{-1}.

***N*-(Phenylpyruvoyl)-L-leucine Ethyl Ester (XIa).** To a solution of X (1 g) in tetrahydrofuran (10 m*l*) was added a solution of sodium bicarbonate (0.24 g) in water (10 m*l*) and methanol (2 m*l*). The resultant clear solution was stirred for 2 hr and concentrated. The residue was dissolved in ether and treated with 1 N hydrochloric acid. The ethereal layer was washed twice with water and dried over anhydrous sodium sulfate. Removal of the ether gave the product (0.8 g, 91%) as a pale yellow oil, which was used without further purification.

IR: 3300 (NH), 1740 (COOEt), 1700 (COCO), 1530, 1200 and 700 cm^{-1}.

2,4-Dinitrophenylhdrazone of XIa. Orange prisms from ethanol, mp 156—157°C.

Found: C, 56.73; H, 5.35; N, 14.53%. Calcd for $C_{23}H_{27}N_5O_7$: C, 56.90; H, 5.61; N, 14.43%.

***N*-(Phenylpyruvoyl)-L-leucine Methyl Ester (XIb).** A solution of *N*-phenylpyruvoyl-L-leucine[1] (3.0 g) in methanol (30 m*l*) was refluxed in the presence of *p*-toluenesulfonic acid (0.5 g) for 4 hr and concentrated. Ether was added to the residue and then insoluble crystalline precipitates were filtered off. The ethereal filtrate was washed twice with water and dried over anhydrous sodium sulfate. Evaporation of the ether gave a pale yellow oily product (2.3 g, 73%), a portion of which was converted into the 2,4-dinitrophenylhydrazone.

IR: 3300 (NH), 1740 (COOMe), 1685 (COCO), 1530 (CONH), 1200, 1150 and 700 cm^{-1}.

2,4-Dinitrophenylhydrazone of XIb. Yellow prisms from methanol, mp 161°C.

3-Benzylidene-6-isobutyl-2,5-piperazinedione (XII). *From XIa.* A solution of the crude XIa (1 g) in methanol (20 m*l*) was saturated with gaseous ammonia under cooling and allowed to stand at room temperature for 24 hr. The crystalline precipitates were collected

14) R. Hemmerlé, *Ann. chim. (Paris)*, **7**, 226 (1917).

15) Z. Jerzmanowska and L. Pijewska, *Roczniki Chem.*, **36**, 653 (1962); *Chem. Abstr.*, **59**, 523 (1963).

and sublimed at 230°C under reduced pressure (2 mmHg). Recrystallization of the product from ethanol gave colorless needles (0.2 g, 24%), mp 237—238°C.

Found: C, 69.73; H, 6.70; N, 11.25%. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.85%.

IR (KBr): 3200, 3050 (2NH), 1680 (C=C), 1630 (CONH), 1440, 1390 and 700 cm^{-1}.

From XIb. The crude XIb (1.5 g) in methanol (20 m*l*) was treated with gaseous ammonia in a manner analogous to the case of XIa to yield 0.4 g (30%) of the product. The product was identical, in melting point and infrared spectrum with the sample obtained from XIa.

From X. The piperazinedione (XII) was obtained in 15% yield from X by treating with ammonia in a manner analogous to the case of XIa.