[Chem. Pharm. Bull. 19(12)2603—2608(1971)]

UDC 547.94.057 : 547.586.2.04

Amino Acids and Peptides. II.[1] A One-Step Synthesis of Atropine and Other Related Alkaloids from *dl*-Phenylalanine 3α-Tropanyl Ester

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(Received June 23, 1971)

Atropine (VI), littorine (VII), apoatropine (IX), and related compounds have been synthesized by a one-step deamination reaction from *dl*-phenylalanine 3α-tropanyl ester (V). The amino ester (V) was obtained by coupling tropine with N-phthalyl-*dl*-phenylalanyl chloride (III) followed by hydrazinolysis with an equimolar amount of hydrazine hydrate.

Tropic acid (I), the acid moiety of some ester alkaloids such as hyoscyamine and scopolamine is derived from phenylalanine (II) in plants.[3] On the other hand, I was obtained by chemical deamination of phenylalanine ethyl ester with nitrous acid, followed by hydrolysis *in vitro*.[4] Interestingly, II is transformed to I by different mechanisms *in vivo* and *in vitro*; carboxyl group migration occurs in the former,[5] and phenyl migration in the latter.[4,5]

$C_6H_5\text{-}\underset{\displaystyle CH_2OH}{CH}\text{-}COOH$ I

$C_6H_5\text{-}CH_2\text{-}\underset{\displaystyle NH_2}{CH}\text{-}COOH$ II

Fig. 1

This paper deals with a one-step synthesis of atropine, littorine, apoatropine, and related compounds from *dl*-phenylalanine 3α-tropanyl ester (V). The amino ester (V) was obtained as shown in Chart 1.

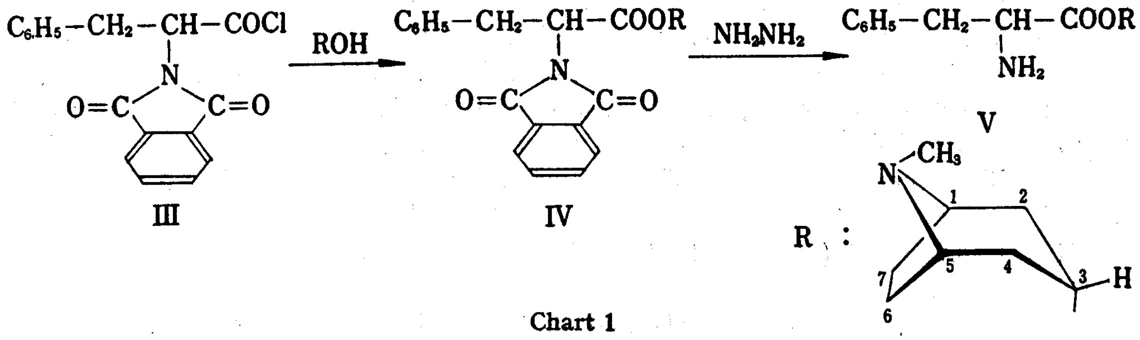

Chart 1

The reaction of N-phthalyl-*dl*-phenylalanyl chloride[6] (III) with tropine[7] gave in 84% yield N-phthalyl-*dl*-phenylalanine 3α-tropanyl ester (IV), mp 133—134°; which after hy-

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[1] Part I: S. Yamada, M. Wagatsuma, Y. Takeuchi, and S. Terashima, *Chem. Pharm. Bull.* (Tokyo), **19**, 2380 (1971).

[2] Location: *Hongo, Bunkyo-ku, Tokyo.*

[3] *a*) M.L. Louden and E. Leete, *J. Am. Chem. Soc.*, **84**, 4507 (1962); *b*) E.W. Underhill and H.W. Youngken, *J. Pharm. Sci.*, **51**, 121 (1962); *c*) D. Gross and H.R. Schütte, *Arch. Pharm.*, **296**, 1 (1963); *d*) H.R. Schütte and H.W. Liebisch, *Z. Pflanzenphysiol.*, **57**, 440 (1967).

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[5] E. Leete, *Tetrahedron Letters*, **1968**, 5793.

[6] J.C. Sheehan, D.W. Chapman, and R.W. Roth, *J. Am. Chem. Soc.*, **74**, 3822 (1952).

[7] L.C. Keagle and W.H. Hartung, *J. Am. Chem. Soc.*, **68**, 1608 (1946).

drazinolysis with an equimolar amount of hydrazine hydrate afforded V without ester group being damaged.[8] Several other routes to V were also investigated, but these resulted in failure.

dl-Phenylalanine 3α-tropanyl ester (V) is a pale yellow liquid, bp 150—167° (0.04 mmHg), whose elementary analysis, infrared (IR) and nuclear magnetic resonance (NMR) spectra support this structure, and its picrate shows mp 112—115°.

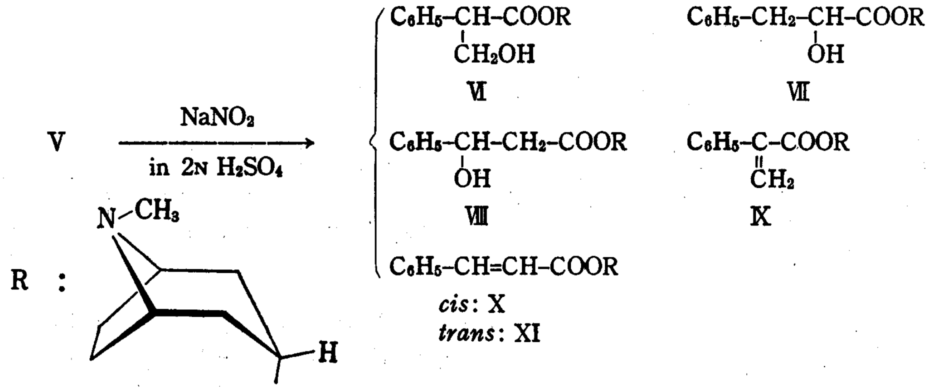

Chart 2

The amino ester (V) was dissolved in 2N H_2SO_4, then sodium nitrite was added to this solution at room temperature. The basic fraction of the reaction mixture was obtained by the usual work up. Six compounds, VI to XI are thought to be present as a mixture in this basic fraction based on a comparison of its NMR spectrum with spectra of authentic samples, VI, VII, IX, and XI, prepared by alternative routes (Chart 2). To separate each, a mixture of reaction products was chromatographed in benzene–chloroform on neutral alumina. Atropine (VI) fractions soon crystallized after evaporation of the solvent. Recrystallization from acetone gave colorless prisms, mp 114.5—115°, which was undepressed by admixture with an authentic sample. Atropine (VI) was formed in about a 20% yield based on the NMR spectrum of a mixture of reaction products.

Besides VI, 3α-tropanyl *dl* 3-hydroxy-3-phenylpropionate (VIII), apoatropine (IX), and 3α-tropanyl *trans*-cinnamate (XI) were also isolated. VIII shows mp 97—101°, NMR (τ, $CDCl_3$): 4.8 (1H, broad, -O$\underline{H}$), 4.99 (1H, q, C_6H_5-C$\underline{H}$-), 7.40 (2H, q, -C$\underline{H}_2$-COO); and elementary analysis satisfied this structure. Two compounds, IX and XI, were identified by comparison with authentic samples. They showed the following data. IX: NMR (τ, $CDCl_3$): 3.67 and 4.15 (2H, two doublets, >C=C$\underline{H}_2$), and its hydrochloride shows mp 242—242.5°. XI: NMR (τ, $CDCl_3$): 2.40 (1H, d, C_6H_5-C$\underline{H}$=CH-), 3.65 (1H, d, -CH=C$\underline{H}$-COO), and its sulfate melts at 225—226°.

Two compounds, *dl*-littorine (VII) and 3α-tropanyl *cis*-cinnamate (X), could not be isolated in a pure state by column chromatography because of their *Rf* values being nearly the same as those of the other compounds (see Experimental; Second part of Deamination Reaction in 2N H_2SO_4). The presence of VII was recognized, however, from NMR spectra of the crude fraction compared with that of an authentic sample. Characteristic signals, (τ, $CDCl_3$) at 5.75 (1H, t, -C$\underline{H}$-COO) and 7.05 (2H, d, C_6H_5-C$\underline{H}_2$-) can be assigned to the structure of VII. The signals (τ, $CDCl_3$) at 3.07 (1H, d, C_6H_5-C$\underline{H}$=CH-) and 4.07 (1H, d, -CH=C$\underline{H}$-COO) can be assigned to the structure of X by comparison with the NMR spectrum of X ($R=C_2H_5$), as reported in our earlier paper.[4]

Product ratios of compounds from VI to XI are approximately the same, and the products, VI and IX, formed by phenyl migration had total yields of 30—40%.

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[8] F.E. King, J.W. Clark-Lewis, D.A.A. Kidd, and G.R. Smith, *J. Chem. Soc.*, **1954**, 1039.

We also examined this deamination reaction in 1 N and 10 N H_2SO_4. The results showed nearly the same pattern as that in 2 N H_2SO_4. But in concentrated 10 N H_2SO_4 solution, the elimination products IX decreased, while atropine (VI) increased. Consequently, total yields of phenyl migration products did not seem to vary with the concentration of H_2SO_4.

Moreover, when the reaction was carried out in AcOH, the presence of the acetyl derivatives, XII and XIII, which correspond to VII and VIII was recognized, as well as IX, X, and XI, in a mixture of reaction products in the NMR spectrum (Chart 3). But acetyl atropine was not detected, probably because of its lability to its eliminated correspondence, apoatropine (IX).

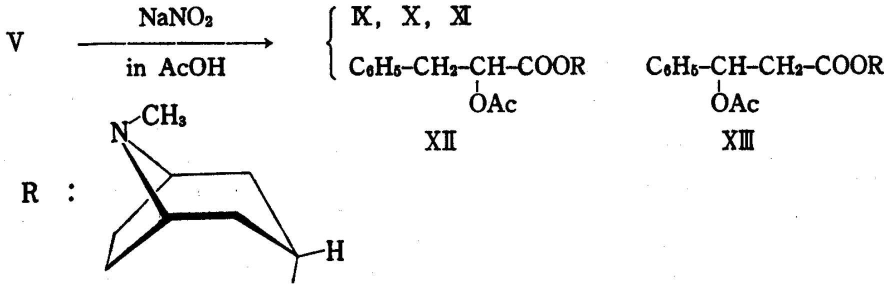

Chart 3

The authentic samples of the deamination products were obtained as follows. Atropine (VI) used in this study came from commercial source. *dl*-Littorine (VII) was prepared by the reaction of tropine with *dl*-2-hydroxy-3-phenylpropionic acid according to the method in the literature.[9] Apoatropine[10] (IX) was obtained in high yield from atropine (VI) by the action of sulfuric acid followed by potassium hydroxide, or by the treatment of acetyl atropine hydrochloride with alkali. 3α-Tropanyl *trans*-cinnamate (XI) was prepared by reacting tropine with *trans*-cinnamoyl chloride according to a procedure similar to IV. Acetyl littorine (XII) and acetyl atropine were prepared by acetylating littorine and atorpine, respectively, according to the general method.

Although VIII, X, and XI have not yet been found in natural sources, VI,[11] VII,[12] and IX[11] are alkaloids isolated from plants. Their acid moieties are reported to be derived from phenylalanine (II) *in vivo*.[4,5,11-13] It is interesting that these three alkaloids are formed from phenylalanine derivative (V) at the same time by a one-step deamination reaction.

Experimental

Synthesis of Starting Material

N-Phthalyl-*dl*-phenylalanyl Chloride (III)——N-Phathalyl-*dl*-phenylalanyl chloride was prepared according to the procedure of Sheehan.[6] The reaction of N-phthalyl-*dl*-phenylalanine with phosphorus pentachloride afforded N-phthalyl-*dl*-phenylalanyl chloride (III) in 88% yield. Recrystallization from benzene–petroleum ether gave colorless needles, mp 130—131° (Lit.[14] mp 124—126°). *Anal.* Calcd. for $C_{17}H_{12}O_3NCl$: C, 65.08; H, 3.86; N, 4.47. Found: C, 65.09; H, 3.97; N, 4.67.

N-Phthalyl-*dl*-phenylalanine 3α-Tropanyl Ester (IV)——The chloride (III) (20 g) was dissolved in absolute benzene (200 ml) and the solution was heated under reflux. When it was completely dissolved tropine[7] (5.5 g) in absolute benzene (50 ml) was added dropwise to this solution and the whole was refluxed for 7 hr. After cooling, the white precipitates were collected by filtration, and were dissolved in H_2O. The solution was

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made alkaline with 10% Na_2CO_3 solution (150 ml), then the aqueous solution was extracted with three 100 ml portions of benzene. Organic layers were washed with sat. NaCl solution and dried over anhyd. $NaSO_4$. Evaporation of benzene to dryness gave a crude product, mp 132—134°. Yield, 13.7 g (84.0%). Recrystallization from EtOH–H_2O gave colorless leaflets, mp 133—134°. IR ν_{max}^{KBr} cm^{-1}: 2800, 1775, 1740, 1720, 1390, 1035, 723. NMR (τ, $CDCl_3$): 2.30 (4H, d, aromatic protons), 2.85 (5H s, aromatic protons), 4.88 (2H, two triplets, C_3 methine in tropane skeleton and $-\underset{|}{C}\underline{H}-COO$), 6.44 (2H, d, $C_6H_5-C\underline{H}_2-$), 6.99 (2H, m, C_1 and C_5 methines in tropane skeleton), 7.81 (3H, s, $\rangle N-C\underline{H}_3$), 7.8—8.7 (8H, m, four methylenes in tropane skeleton).

The picrate of IV was recrystallized from EtOH in yellow needles, mp 229.5—231.5°. *Anal.* Calcd. for $C_{31}H_{29}O_{11}N_5$: C, 57.49; H, 4.51; N, 10.82. Found: C, 57.45; H, 4.61; N, 10.82.

Its methiodide was recrystallized from EtOH in colorless prisms, mp 248—249°.

***dl*-Phenylalanine 3α-Tropanyl Ester (V)**——An ethanolic solution (100 ml) of IV (4.19 g, 0.01 mole) and 90% hydrazine hydrate (0.56 g, 0.01 mole) was refluxed for 6 hr. During this time, the white phthalyl hydrazide precipitated. After cooling, the precipitate was filtered off. Then, the ethanolic solution was evaporated under reduced pressure. To the condensate was added chloroform (100 ml) and insoluble phthalyl hydrazide was again filterd off. The organic layer was washed first with sat. $NaHCO_3$ solution, then with sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a pale yellow oil. Distillation for analytical sample indicated bp 150—167° (0.04 mmHg), and gave a yield of 2.25 g (78.1%). IR ν_{max}^{film} cm^{-1}: 3400, 2800, 1735, 1185, 1035. NMR (τ. $CDCl_3$): 2.85 (5H, s, aromatic protons), 5.09 (1H, t, C_3 methine in tropane skeleton), 6.45 (1H, q, $-\underset{|}{C}\underline{H}-COO$), 6.7—7.5 (4H, m, C_1 and C_5 methines in tropane skeleton and $C_6H_5-C\underline{H}_2-$), 7.6—9.0 (10H, m, four methylenes in tropane skeleton and $-N\underline{H}_2$).

Its picrate was recrystallized from EtOH in yellow prisms, which melted at 112—115°. *Anal.* Calcd. for $C_{29}H_{30}O_{16}N_8$: C, 46.65; H, 4.05; N, 15.01. Found: C, 46.96; H, 4.41; N, 14.98.

Deamination of V

Reaction in 2N H_2SO_4——The amino ester (V) (10.96 g, 0.038 mole) was dissolved in 2N H_2SO_4 (220 ml), then sodium nitrite (11.54 g, 0.167 mole) was added with stirring at room temperature during 7 days. After the reaction mixture was washed with ether (30 ml), the aqueous layer was made alkaline (pH 10) and extracted with four 100 ml portions of chloroform. The organic layers were washed with sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a yellow oil (7.58 g), which was chromatographed in benzene–chloroform (1:1) on neutral alumina (1150 g).

The initially eluted part (Fractions 1—50) were recognized to be a mixture of IX, X, and XI based on their NMR spectra. To separate each, this mixture was again chromatographed in benzene. IX and XI were obtained and identified with authentics samples by comparison of the IR and NMR spectra, respectively. The hydorchloride of IX and the picrate of XI showed mp 241—243° and 246—247°, respectively. These were undepressed by admixture with authentic samples. X was not isolated in a pure form; however, a pair of doublets centered (τ, $CDCl_3$) at 3.07 and 4.07 characterized the structure of *cis*-cinnamate and the preseace of X in the mixture was evident from the NMR spectrum.

The second part (Fractions 51—226) contained VII, VIII, IX, X, and XI. No further separation was successful, yet the signals (τ, $CDCl_3$) at 5.75 (t, $-\underset{|}{C}H-COO$) and 7.05 (d, $C_6H_5-C\underline{H}_2-$) could be assigned to the structure of VII by comparison with the NMR spectrum of an authentic sample.

The third part (Fractions 227—229) contained VIII only. Evaporation of the solvent gave a colorless solid. Recrystallization from hexane gave pure VIII in yellow leaflets, mp 97—101°. IR ν_{max}^{Nujol}cm^{-1}: 2800, 1730, 1470, 1028, 695. NMR (τ, $CDCl_3$): 2.75 (5H, s, aromatic protons), 4.99 (1H, q, $C_6H_5-\underset{|}{C}\underline{H}-$), 5.81 (1H, t, C_3 methine in tropane skeleton), 7.10 (2H, s, C_1 and C_5 methines in tropane skeleton), 7.40 (2H, q, $-C\underline{H}_2-COO$), 7.92 (3H, s, $\rangle N-C\underline{H}_3$), 7.6—8.9 (8H, m, four methylenes in tropane skeleton).

The last part (Fractions 235—254) mainly contained atropine (VI). Recrystallization from acetone gave colorless prisms, mp 114.5—115°, which was undepressed by admixture with an authentic sample. IR ν_{max}^{KBr} cm^{-1}: 2810, 1730, 1155, 1035, 695. NMR (τ, $CDCl_3$): 2.77 (5H, aromatic protons), 5.05 (1H, t, C_3 methine in tropane skeleton), 5.50 (1H, broad, $-O\underline{H}$), 5.6—6.5 (3H, m, $-\underset{|}{C}\underline{H}-C\underline{H}_2-OH$), 7.05 (2H, s, C_1 and C_5 methines in tropane skeleton), 7.85 (3H, s, $\rangle N-C\underline{H}_3$), 7.6—9.2 (8H, m, four methylenes in tropane skeleton). *Anal.* Calcd. for $C_{17}H_{23}O_3N$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.69; H, 7.95; N, 4.92.

Deamination reactions in 1N- and 10N H_2SO_4 were carried out under reaction conditions similar to those above.

Reaction in AcOH——The amino ester (V) (5.78 g, 0.02 mole) was dissolved in AcOH (100 ml), then sodim nitrite (1.52 g, 0.022 mole) was added to this solution with stirring at room temperature for 4 hr. The resulting solution was stirred overnight, then the solvent was evaporated to dryness *in vaccuo*. After the residue was dissolved in 10% Na_2CO_3 solution (100 ml), products were extracted with three 100 ml portions of chloroform. Organic layers were washed sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a yellow oil (6.68 g), whose NMR spectrum suggested the presence of five compounds, IX to XIII. The characteristic signals (τ, $CDCl_3$) at 3.67 and 4.15 (two doublets, $\rangle C=C\underline{H}_2$), at 2.38 (d, $C_6H_5-C\underline{H}=CH-$) and 3.65 (d, $-CH=C\underline{H}-COO$), and at 4.92 (t, $-\underset{|}{C}\underline{H}-COO$) can be assigned, respectively, to the structures of IX, XI, and XII by comparison with NMR spectra of authentic samples. Moreover, signals (τ, $CDCl_3$) at 3.07 (d, $C_6H_5-C\underline{H}=CH-$) at 4.07 (d, $-CH=C\underline{H}-COO$) and at 4.45 (q, $C_6H_5-\underset{|}{C}\underline{H}-$) can be assigned, respectively, to the structures of X and XIII by comparison with NMR spectra of X ($R=C_2H_5$) and XIII ($R=C_2H_5$) reported in an earlier paper.4) The expected acetyl atropine was not detected in the NMR spectrum of the reaction mixture.

Synthesis of Authentic Samples

***dl*-Littorine: 3α-Tropanyl *dl*-2-Hydroxy-3-phenylpropionate (VII)**9)——*dl*-2-Hydroxy-3-phenylpropionic acid15) (3.5 g, 0.021 mole) and tropine7) (2.5 g. 0.018 mole) were heated for 5 hr at 130° in a stream of dry hydrogen chloride. The resulting gum was decomposed with 10% ammonium hydroxide (100 ml) and extracted with chloroform, from which the alkaloid was then extracted with 10% hydrochloric acid. After regeneration with sodium carbonate and extraction with four 100 ml protions of ether, the organic layers were washed with sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a colorless oil. Yield, 2.96 g (56.9%). IR ν_{max}^{film} cm^{-1}: 3300, 2800, 1740, 1195, 1035, 750, 695. NMR (τ, $CDCl_3$): 2.83 (5H, s, aromatic protons), 4.65 (1H, broad, $-O\underline{H}$), 5.08 (1H, t, C_3 methine in tropane skeleton), 5.75 (1H, t, $-\underset{|}{C}\underline{H}-COO$), 7.05 (4H, d, C_1 and C_5 methines in tropane skeleton and $C_6H_5-\underline{CH_2}-$), 7.85 (3H, s, $>N-\underline{CH_3}$), 7.5—8.9 (8H, m, four methylenes in tropane skeleton).

The sulfate of VII was recrystallized from EtOH–acetone in colorless prisms, which melted at 197—198°. *Anal.* Calcd. for $C_{17}H_{23}O_3N \cdot 1/2H_2SO_4$: C, 60.33; H, 7.15; N, 4.14. Fouod: C, 60.11; H, 7.06; N, 4.40.

Its picrate was recrystallized from EtOH in yellow needles, which melted at 158—158.5° (Lit.9) 159—160°).

Apoatropine (IX)——The procedure used was a modification of the method of Maeda.10) Atropine (1.45 g, 0.005 mole) was dissolved in conc. H_2SO_4 (2 g) and the mixture was allowed to stand for 2 hr at room temperature. Then, finely cracked ice (5 g) was carefully added in small portions to this solution under cooling. After regeneration with 10% KOH solution, apoatropine was extracted with ether (50 ml) three times. The ether layers were washed with sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a colorless oil, which crystallized on standing, mp 59—60° (Lit.16) mp 60°). Yield, 1.24 g (91.4%). IR ν_{max}^{Nujol} cm^{-1}: 2800, 1705, 1200, 1030, 695. NMR (τ, $CDCl_3$): 2.68 (5H, s, aromatic protons), 3.67 and 4.15 (2H, tow doublets, $>C=\underline{CH_2}$), 4.87 (1H, t, C_3 methine in tropane skeleton), 6.83 (2H, s, C_1 and C_5 methines in tropane skeleton), 7.70 (3H, s, $>N-\underline{CH_3}$), 7.4—8.8 (8H, m, four methylenes in tropane skeleton).

The hydrochloride of IX was recrystallized form EtOH in colorless needles, which melted at 242—243° (Lit.17) mp 245—246°). *Anal.* Calcd. for $C_{17}H_{21}O_2N \cdot HCl$: C, 66.33; H, 7.20; N, 4.55. Found: C, 66.05; H, 7.33; N, 4.76.

Apoatropine was also obtained by the reaction of acetyl atropine hydrochloride with alkali. Acetyl atropine hydrochloride (1.10 g, 0.003 mole) was dissloved in H_2O (10 ml) and the solution was made alkaline with 10% KOH solution (50 ml). The aqueous solution was then extracted with three 50 ml portions of ether. Evaporation of the solvent gave a colorless solid, mp 59°. Yield, 0.81 g (87.8%).

3α-Tropanyl *trans*-Cinnamate9) **(XI)**——Cinnamoyl chloride18) (11.66 g, 0.07 mole) was dissolved in absolute benzene (150 ml) and the solution was heated under reflux. Tropine (4.23 g, 0.03 mole) in absolute benzene was added dropwise to this solution over 10 min and the mixture was refluxed for 30 min. After cooling, the white precipitates were collected on a filter, then were dissolved in 10% Na_2CO_3 aqueous solution (100 ml) and extracted with four 100 ml portions of ether. Organic layers were washed with sat. NaCl solution and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a pale yellow oil. Yield, 6.05 g (74.3%). IR ν_{max}^{film} cm^{-1}: 2800, 1710, 1640, 1175, 1035, 770. NMR (τ, $CDCl_3$): 2.38 (1H, d, $C_6H_5-\underline{CH}=CH-$), 2.60 (5H, m, aromatic protons), 3.65 (1H, d, $-CH=\underline{CH}-COO$), 4.86 (1H, t, C_3 methine in tropane skeleton), 6.75 (2H, s, C_1 and C_5 methines in tropane skeleton), 7.63 (3H, s, $>N-\underline{CH_3}$), 7.3—8.5 (8H, m, four methylenes in tropane skeleton).

The picrate of XI was recrystallized from EtOH–ether in yellow needles, which melted at 248.5—250° (Lit.9) 244—245°). *Anal.* Calcd. for $C_{23}H_{24}O_9N_4$: C, 55.20; H, 4.83; N, 11.20. Found: C, 54.97; H, 5.05; N, 11.43.

Its sulfate was recrystallized from EtOH–ether in colorless leaflets, which melted at 225—226° (Lit.9) 227—229°).

3α-Tropanyl *dl*-2-Acetoxy-3-phenylpropionate (XII)——A mixture of 3α-tropanyl *dl*-2-hydroxy-3-phenylpropionate (VII) (1 g, 0.0034 mole), acetic anhydride (2 ml), and pyridine (10 ml) was left at room temperature for 2 days, then the mixture was heated at 90° for 3 hr. Evaporation of the solvent under reduced pressure gave a brown oil, which was dissolved in 10% Na_2CO_3 solution (50 ml) and extracted with three 50 ml portions of chloroform. Organic layers were washed with sat. NaCl solution then dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a pale yellow oil. Yield, 0.94 g (82.1%). IR ν_{max}^{film} cm^{-1}: 2800, 1740, 1230, 700. NMR (τ, $CDCl_3$): 2.85 (5H, s, aromatic protons), 4.92 (1H, t, $-\underset{|}{C}\underline{H}-COO$), 5.10 (1H, t, C_3 methine in tropane skeleton), 6.95 (4H, d, C_1 and C_5 methines in tropane skeleton and $C_6H_5-\underline{CH_2}-$), 7.85 (3H, s, $>N-\underline{CH_3}$), 8.00 (3H, s, $-OCO\underline{CH_3}$), 7.5—8.9 (8H, m, four methylenes in tropane skeleton).

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Its picrate was recrystallized from EtOH in yellow leaflets, which melted at 144.5—146°. *Anal.* Calcd. for $C_{25}H_{28}O_{11}N_4$: C, 53.56; H, 5.22; N, 10.00. Found: C, 53.16; H, 5.03; N, 10.20.

Acetyl Atropine Hydrochloride——To the solution of atropine (1.73 g, 0.006 mole) in absolute benzene (80 ml) was dropwise added acetyl chloride (0.78 g, 0.01 mole) under stirring. The resulting mixture was heated under reflux for 10 min then precipitates were collected on a filter after cooling. Recrystallization from EtOH–ether gave colorless prisms, mp 156—157.5°. Yield, 1.81 g (81.9%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2800, 1735, 1240, 1925, 700. NMR (τ, D_2O): 2.70 (5H, s, aromatic protons), 4.95 (1H, t, C_3 methine in tropane skeleton), 5.3—6.5 (3H, m, $-\underset{|}{\mathrm{C}}\underline{\mathrm{H}}-\mathrm{COO}$ and $-\mathrm{C}\underline{\mathrm{H}}_2-\mathrm{OCO}$), 7.15 (2H s, C_1 and C_5 methines in tropane skeleton), 7.23 (3H, s, $\rangle\mathrm{N}-\mathrm{C}\underline{\mathrm{H}}_3$), 7.98 (3H, s, $-\mathrm{OCOC}\underline{\mathrm{H}}_3$), 7.5—8.7 (8H, m, four methylenes in tropane skeleton). *Anal.* Calcd. for $C_{19}H_{25}O_4N \cdot HCl$: C, 62.03; H, 7.12; N, 3.81. Found: 61.73; H, 7.19; N, 3.51.

When acetyl atropine hydrochloride was treated with alkali, no more free acetyl atropine was obtained, while the eliminated product, apoatropine (IX), was formed.