Synthesis and Reactions of Ethyl 3-Acetyl-8-cyano-6,7-dimethylpyrrolo[1,2-*a*]pyrimidine-4-carboxylate and Related Compounds

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The reactions of 3-acetyl-4-ethoxycarbonyl- or 3,4-diethoxycarbonylpyrrolo[1,2-*a*]pyrimidine derivatives **7a,b**, which were prepared by condensation of the 2-aminopyrrole (**4**) with ethyl 3-ethoxymethylene-2,4-dioxovalerate (**5a**) or ethyl ethoxymethyleneoxaloacetate (**5b**), with diazomethane are described. Thus, reaction of **7a** with diazomethane gave ethyl 2a-acetyl-7-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]pyrrolo-[1,2-*a*]pyrimidine-3a-carboxylate (**11**) in 74% yield, which was readily transformed into the 1-pyrrol-2-yl-pyrrole (**18**) by treatment with potassium hydroxide. On the other hand, reaction of **7b** with diazomethane afforded three products whose structures were assigned as diethyl 7-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]pyrrolo[1,2-*a*]pyrimidine-2a,3a-dicarboxylate (**20**), diethyl 6-cyano-7,8-dimethyl-3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-1*H* or 3*H*-pyrazolo[3,4-*e*]pyrrolo[1,2-*a*]pyrimidine-3a,9a-dicarboxylates (**21**, **22**). Ring transformation of **20** to **25** was not observed.

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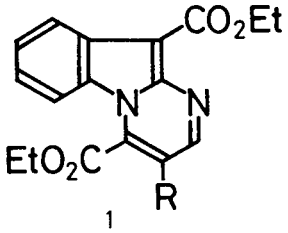
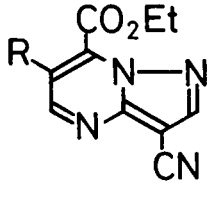
In previous papers (1) we reported the synthesis and some chemical reactivities (for example; hydrogenation, reaction with diazomethane, nucleophilic substitution) of the condensed pyrimidine heterocycles having two carbonyl functional groups on the pyrimidine ring, such as pyrimido[1,2-*a*]indoles **1**, pyrazolo[1,5-*a*]pyrimidines **2**, and imidazo[1,2-*a*]pyrimidines **3**. On the continuation of our further exploring an analogous reaction of the condensed pyrimidines, the utilization of pyrrolo[1,2-*a*]pyrimidine derivatives to lead other heterocycles was examined.

Chart 1

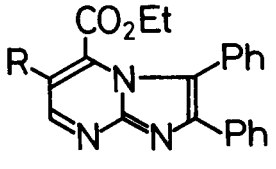


1



2

R=COMe or CO_2Et



3

No biological activity has been reported for pyrrolo-[1,2-*a*]pyrimidines, but partially saturated derivatives have been shown interest as catalyst for polyurethane manufacture (2). Although Blanton, *et al.* (3) reported the facile route for the synthesis of pyrolo[1,2-*a*]pyrimidine derivatives, few examples have been reported for the preparation of pyrrolo[1,2-*a*]pyrimidines (4).

Reaction of 2-amino-3-cyano-4,5-dimethylpyrrole (**4**) (5) with ethyl 3-ethoxymethylene-2,4-dioxovalerate (**5a**) or ethyl ethoxymethyleneoxaloacetate (**5b**) in ethanol under ice cooling gave the 2-pyrrolylaminomethylene derivatives **6a,b** in good yields, respectively. Cyclization by refluxing **6a** in ethanol afforded the desired ethyl 3-acetyl-8-cyano-6,7-dimethylpyrrolo[1,2-*a*]pyrimidine-4-carboxylate (**7a**) in 60% yield, together with 4% yield of ethyl 8-cyano-4,6,7-trimethylpyrrolo[1,2-*a*]pyrimidine-3-glyoxylate (**8**). On the other hand, refluxing **6b** in ethanol gave diethyl 8-cyano-6,7-dimethylpyrrolo[1,2-*a*]pyrimidine-3,4-dicarboxylate (**7b**) in 81% yield as a sole product. Catalytic hydrogenation of **7a,b** over 5% palladium-carbon afforded the 1,4-dihydropyrimidines **9a,b**, but compound **8** was recovered unchanged under the same conditions. In order to confirm the structural assignment, **8** was treated with phenylhydrazine hydrochloride to give α-phenylhydrazono derivatives **10**.

Treatment of **7a** with an excess diazomethane at room temperature gave ethyl 2a-acetyl-7-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]pyrrolo[1,2-*a*]pyrimidine-3a-carboxylate (**11**) in 74% yield. The structure of **11** was determined from its proton magnetic resonance (pmr) spectrum, which exhibited signals due to the cyclopropane ring protons at 1.41 and 2.72 ppm as a doublet with a coupling constant (J) of 6 Hz. On catalytic hydrogenation in the presence of 5% palladium-carbon under atmospheric pressure, the hydrogenolysis of the cyclopropane ring of **11** was effected in two ways to give a mixture of **12** (46%) and **13** (18%). Based on the analytical and spectral data detailed in the experimental section, the 4,5-dihydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepine and the 1,4-dihydro-4-

Chart 2

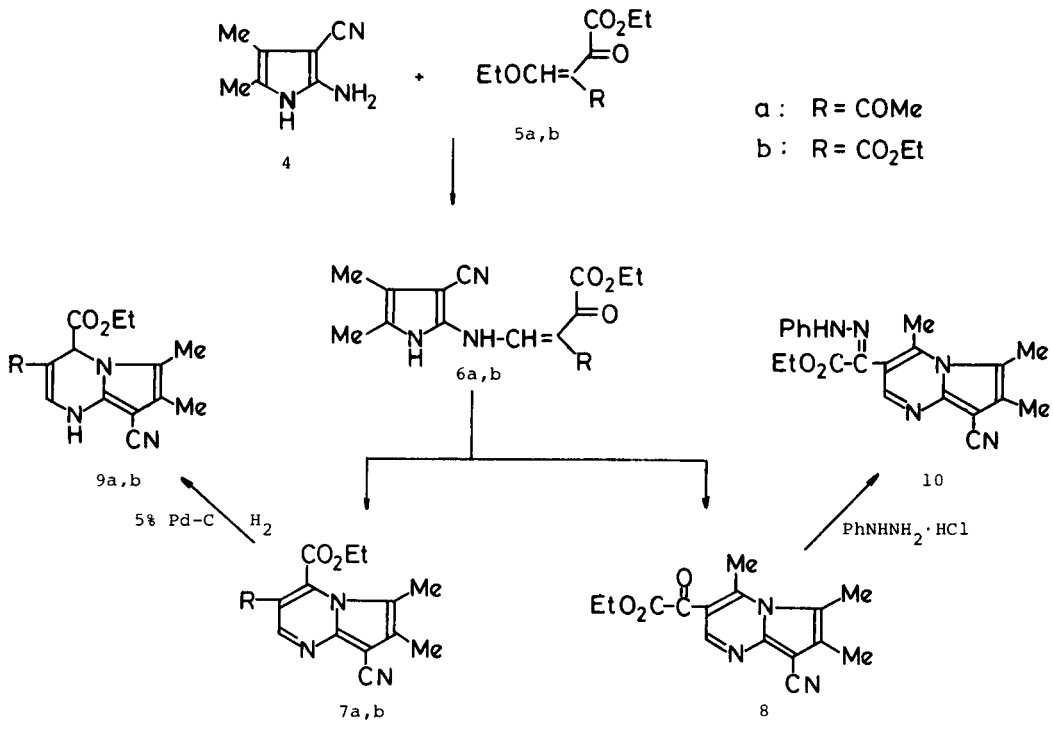
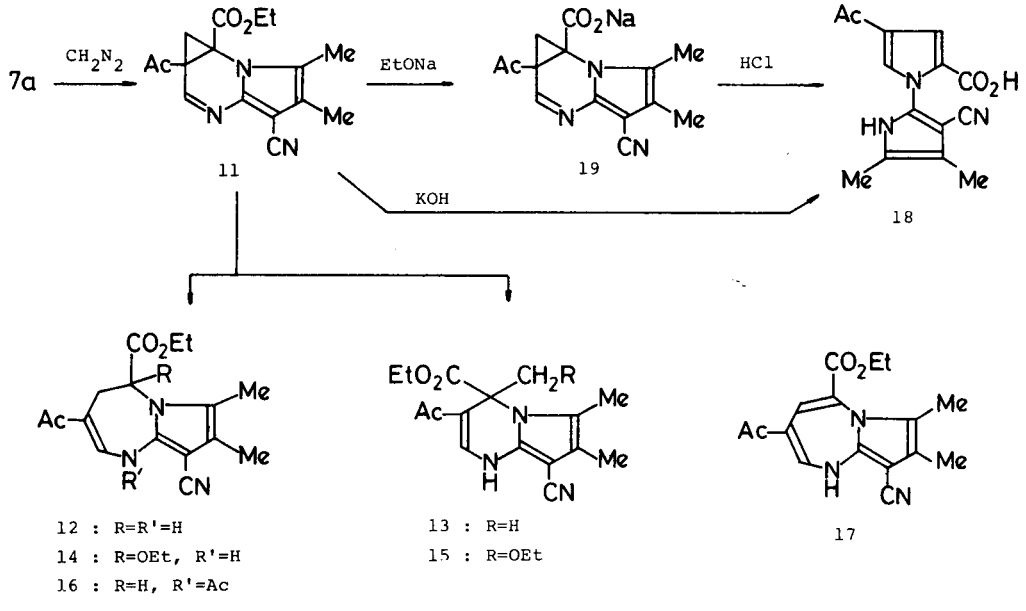
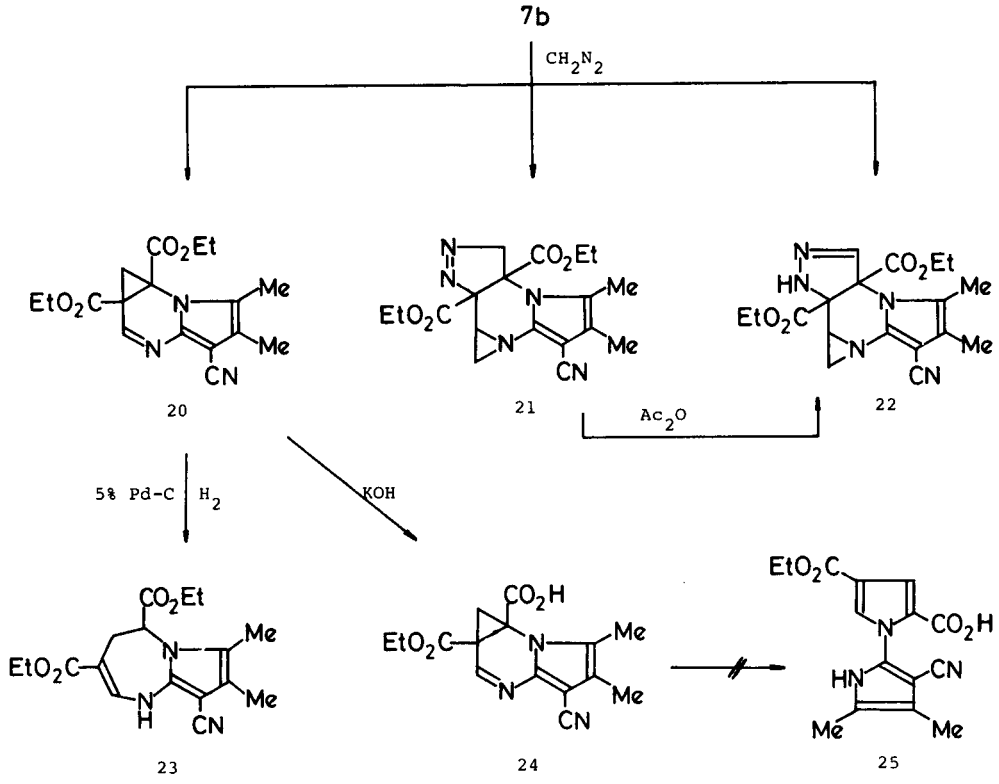


Chart 3



methylpyrrolo[1,2-*a*]pyrimidine structures were assigned to the products **12** and **13**. When refluxed in ethanol for 10 days, **11** reacted with ethanol to give a mixture of the 4,5-dihydro-5-ethoxy-1*H*-pyrrolo[1,2-*a*][1,3]diazepine (**14**) (7%) and the 1,4-dihydro-4-ethoxymethylpyrrolo[1,2-*a*]pyrimidine (**15**) (38%). Recently we reported (6) the synthesis of 9*H*-imidazo[1,2-*a*][1,3]diazepine *via* the ring expansion of 5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine followed by bromination and subsequent dehydrobromination. Attempt to synthesize the 1*H*-pyrrolo[1,2-*a*][1,3]diazepine (**17**) under the same route failed, only tarry mixture being obtained. Treatment of **11** with equimolar amount of potassium hydroxide in aqueous ethanol at room temperature gave a carboxylic acid $C_{14}H_{13}N_3O_3$, as colorless

Chart 4



needles of mp 255-258° in 80% yield. The product exhibited the presence of two aromatic protons in the molecule, showing signals at 7.27 and 7.98 ppm (each 1H, each d, J = 3 Hz), in its pmr spectrum. The ultraviolet (uv) spectrum of the product showed the close similarity with that of 1-pyrazol-3-ylpyrrole (7). On basis of these spectral data, the structure of the product was assigned as 4-acetyl-1-(3-cyano-4,5-dimethylpyrrol-2-yl)pyrrole-2-carboxylic acid (**18**). In addition, treatment of **11** with sodium ethoxide in ethanol under ice cooling afforded the corresponding mono-sodium salt **19**, which was then transformed into 1-pyrrol-2-ylpyrrole (**18**) by just treatment with hydrochloric acid. We have been reported the interesting ring transformations of 6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]pyrimidines (7). Thus, the compound **18** would be formed through similar reaction mechanism.

Next, reaction of **7b** with an excess of diazomethane at room temperature gave three products, pale yellow needles of mp 103-104° ($C_{17}H_{19}N_3O_4$) (**20**), colorless needles of mp 151-152° ($C_{18}H_{21}N_5O_4$) (**22**), in yields of 40, 10, and 19%, respectively. The structural assignment of **20** was readily made on the basis of the results of elemental analysis and by comparison of the pmr spectral data with that of **11**. The pmr spectra of **21** and **22** showed characteristic signals due to the aziridine ring protons [2.52 and 2.73 ppm (each 1H, each d, J = 4 and 5 Hz) and 4.04 ppm (1H, d of d, J = 4, 5 Hz) of **21**, and 2.53 and 2.64 ppm (each 1H, each d, J = 4 and 5 Hz), and 3.03 (1H, d of d, J = 4, 5 Hz) of **22**]. In addition, although **21** showed pyrazoline ring methylene protons at 5.31 and 5.57 ppm (each 1H, each d, J = 18 Hz), a pyrazole ring proton at 6.98 ppm as singlet as well as ring NH proton at 6.70 ppm were observed in **22** in their pmr spectra. Compound **21** was transformed into **22** by treatment with acetic anhydride and pyridine followed by purification with silica gel column chromatography in low yield. Based on these results described above, the 3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-1*H*- or 3*H*-pyrazolo[3,4-*e*]pyrrolo[1,2-*a*]pyrimidine structures were assigned to the products **21** and **22**. When hydrogenated over 5% palladium-carbon, **20** gave the 4,5-dihydro-1*H*-imidazo[1,2-*a*][1,3]diazepine (**23**) in 37% yield. In contrast with **11**, **20** afforded the corresponding carboxylic acid **24** by treatment with potassium hydroxide. Ring transformation of **24** to **25** was unsuccessful, only starting material being recovered.

EXPERIMENTAL

All melting points were recorded on a Yanagimoto micromelting point apparatus and are uncorrected. The ir spectra (potassium bromide) were recorded with a JASCO model IRA-1 spectrophotometer and the uv spectra with a JASCO UVIDEC-505 spectrophotometer. The pmr spectra

were recorded in deuteriodimethylsulfoxide (unless otherwise noted) with a Hitachi R-40 spectrometer with tetramethylsilane as an internal standard.

Ethyl 3-(3-Cyano-4,5-dimethyl-2-pyrroylamino)methylene-2,4-dioxovalerate (**6a**) and Ethyl 3-Cyano-4,5-dimethyl-2-pyrroylaminomethyleneoxaloacetate (**6b**).

A solution of 0.01 mole of **5a** (or **5b**) in 5 ml of ethanol was added to a stirred solution of 0.01 mole of 2-amino-3-cyano-4,5-dimethylpyrrole (**4**) in 50 ml of ethanol with cooling in an ice bath. After stirring had been continued for 2 hours, the yellow precipitate was collected, washed with cold ethanol, and dried. These products were determined by elemental analysis without recrystallization.

Compound **6a** was obtained as a yellow powder, mp 172-174°, yield 86%, ir: ν cm^{-1} 3360 (NH), 2200 (CN), 1710 (CO); pmr: δ 1.27 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.01 and 2.15 (each 3H, each s, 2 × CH_3), 2.30 (3H, s, $COCH_3$), 4.24 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 8.05 (1H, d, J = 13 Hz, =CH), 11.82 (1H, bs, NH), 12.26 (1H, d, J = 13 Hz, NH).

Anal. Calcd. for $C_{15}H_{17}N_3O_4$: C, 59.39; H, 5.65; N, 13.86. Found: C, 59.20; H, 5.72; N, 14.01.

Compound **6b** was obtained as a yellow powder, mp 158-159°, yield, 79%; ir: ν cm^{-1} 3360 (NH), 2200 (CN), 1710 and 1690 (CO); pmr: δ 1.17-1.38 (6H, m, 2 × $CO_2CH_2CH_3$), 2.01 and 2.12 (each 3H, each s, 2 × CH_3), 4.06-4.39 (4H, m, 2 × $CO_2CH_2CH_3$), 8.05 (1H, bs, =CH), 11.87 (1H, bs, NH), 12.30 (1H, bs, NH).

Anal. Calcd. for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61. Found: C, 57.90; H, 5.79; N, 12.70.

Cyclization of **6a** in Refluxing Ethanol.

A solution of 3.03 g (0.01 mole) of **6a** in 100 ml of ethanol was refluxed for 2 days. After removal of the solvent by evaporation, the residue was recrystallized from ethanol to give 1.69 g (60%) of ethyl 3-acetyl-8-cyano-6,7-dimethylpyrrolo[1,2-*a*]pyrimidine-4-carboxylate (**7a**) as yellow needles, mp 155-156°; ir: ν cm^{-1} 2220 (CN), 1730 and 1690 (CO); pmr: δ 1.40 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.35 and 2.37 (each 3H, each s, 2 × CH_3), 2.71 (3H, s, $COCH_3$), 4.51 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 8.95 (1H, s, C(2)-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.97; H, 5.57; N, 14.67.

The filtrate was concentrated *in vacuo*, and the residue was repeatedly recrystallized from ethanol to give 103 mg (4%) of ethyl 8-cyano-4,6,7-trimethylpyrrolo[1,2-*a*]pyrimidine-3-glyoxylate (**8**) as yellow needles, mp 139-140°; ir: ν cm^{-1} 2220 (CN), 1720 and 1680 (CO); pmr: δ 1.42 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.36 and 2.75 (each 3H, each s, C(6)- and C(7)-CH_3), 3.14 (3H, s, C(4)-CH_3), 4.42 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 8.30 (1H, s, C(2)-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.01; H, 5.22; N, 14.71.

Ethyl 3-Acetyl-8-cyano-1,4-dihydro-6,7-dimethylpyrrolo[1,2-*a*]pyrimidine-4-carboxylate (**9a**) and Diethyl 8-Cyano-1,4-dihydro-6,7-dimethylpyrrolo-[1,2-*a*]pyrimidine-3,4-dicarboxylate (**9b**).

A solution of 0.01 mole of **7a** (or **7b**) in 200 ml of methanol was shaken with hydrogen over 1.0 g of 5% palladium-carbon using a Skita apparatus for 12 hours. The reaction mixture was filtered and concentrated *in vacuo* to give **9a** (or **9b**), which were recrystallized from ethanol.

Compound **9a** was obtained as pale yellow plates, mp 198-200°, yield, 60%; ir: ν cm^{-1} 2200 (CN), 1740 (CO); pmr (deuteriochloroform): δ 1.25 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.06 and 2.16 (each 3H, each s, 2 × CH_3), 2.34 (3H, s, $COCH_3$), 4.18 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 5.79 (1H, s, C(4)-H), 7.50 (1H, d, J = 1 Hz, C(2)-H), 9.31 (1H, d, J = 1 Hz, NH).

Anal. Calcd. for $C_{15}H_{17}N_3O_3$: C, 62.70; H, 5.96; N, 14.63. Found: C, 62.58; H, 5.99; N, 14.63.

Compound **9b** was obtained as pale yellow needles of mp 161-162°, yield, 52%; ir: ν cm^{-1} 2200 (CN), 1740 and 1710 (CO); pmr (deuteriochloroform): δ 1.15-1.37 (6H, m, 2 × $CO_2CH_2CH_3$), 2.03 and 2.10 (each 3H, each s, 2 × CH_3), 4.02-4.31 (4H, m, 2 × $CO_2CH_2CH_3$), 5.53 (1H, s, C(4)-H), 7.44 (1H, d, J [5] 6 Hz, C(2)-H), 8.66 (1H, d, J [5] 6 Hz, NH).

Anal. Calcd. for $C_{16}H_{19}N_3O_4$: C, 60.55; H, 6.04; N, 13.24. Found: C, 60.74; H, 6.04; N, 13.22.

Ethyl 8-Cyano-4,6,7-trimethylpyrrolo[1,2-*a*]pyrimidine-3-α-phenylhydrazonoglyoxylate (**10**).

A solution of 285 mg (1 mmole) of **8** and 145 mg (1 mmole) of phenylhydrazine hydrochloride in 50 ml of ethanol was refluxed for 2 hours. After removal of the solvent by evaporation, the residue was recrystallized from ethanol to give 100 mg (27%) of **10** as pale yellow needles, mp 195-197°; ir: ν cm^{-1} 2220 (CN), 1680 (CO); pmr (deuteriochloroform): δ 1.31 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.39 (3H, s, C(4)-CH_3), 2.76 and 2.86 (each 3H, each s, C(6)- and C(7)-CH_3), 4.32 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 7.27 (5H, m, Ar-H), 8.15 (1H, s, C(2)-H), 12.71 (1H, s, NH).

Anal. Calcd. for $C_{21}H_{21}N_5O_2$: C, 67.18; H, 5.64; N, 18.66. Found: C, 67.30; H, 5.54; N, 18.69.

Ethyl 2a-Acetyl-6-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]-pyrrolo[1,2-*a*]pyrimidine-3a-carboxylate (**11**).

Compound **7a** (5.7 g, 0.02 mole) was added to 200 ml of an ethereal solution containing excess diazomethane (prepared from 21 g of *N*-nitrosomethylurea) (8) and the suspension was stirred for 3-4 hours at room temperature. The precipitate was collected and recrystallized from benzene-ligroin to give 4.44 g (74%) of **11** as yellow needles, mp 140-142°; ir: ν cm^{-1} 2220 (CN), 1750 and 1710 (CO); pmr: δ 1.19 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 1.41 and 2.72 (each 1H, each d, J = 6 Hz, CH_2), 2.06 and 2.10 (each 3H, each s, 2 × CH_3), 2.43 (3H, s, $COCH_3$), 4.0-4.40 (2H, m, $CO_2CH_2CH_3$), 8.24 (1H, s, C(2)-H).

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.28; H, 5.75; N, 14.27.

Catalytic Hydrogenation of **11**.

A solution of 2.99 g (0.01 mole) of **11** in 200 ml of ethanol was shaken with hydrogen over 1.5 g of palladium-carbon for 24 hours using a Skita apparatus. The reaction mixture was filtered and concentrated *in vacuo*, then the residue was recrystallized from ethanol to give 1.39 g (46%) of ethyl 3-acetyl-9-cyano-4,5-dihydro-7,8-dimethyl-1*H*-pyrrolo[1,2-*a*][1,3]diazepine-5-carboxylate (**12**) as colorless needles, mp 235-237°; ir: ν cm^{-1} 2220 (CN), 1735 (CO); pmr: δ 1.06 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 1.97 and 2.06 (each 3H, each s, 2 × CH_3), 2.17 (3H, s, $COCH_3$), 2.36 (1H, d of d, J = 3, 18 Hz, C(4)-H), 3.71 (1H, d of d, J = 6, 18 Hz, C(4)-H), 3.90-4.23 (2H, m, $CO_2CH_2CH_3$), 5.44 (1H, d, J = 2 Hz, (C(2)-H), 9.82 (1H, d, J = 2 Hz, NH); uv (ethanol): λ max nm (log ϵ) 354 (3.97).

Anal. Calcd. for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.36; N, 13.95. Found: C, 63.51; H, 6.46; N, 13.96.

The filtrate was concentrated *in vacuo* and the residue was subjected to silica gel column chromatography. Elution with benzene gave 550 mg (18%) of ethyl 3-acetyl-8-cyano-1,4-dihydro-4,6,7-trimethylpyrrolo[1,2-*a*]-pyrimidine-4-carboxylate (**13**) as pale yellow needles, mp 225-226° (from ethyl acetate); ir: ν cm^{-1} 3180 (NH), 2200 (CN), 1730 (CO); pmr: δ 1.15 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 1.61 (3H, s, C(4)-CH_3), 1.98 (6H, s, 2 × CH_3), 2.21 (3H, s, $COCH_3$), 4.0-4.37 (2H, m, $CO_2CH_2CH_3$), 7.55 (1H, bs, C(2)-H), 10.95 (1H, bs, NH); uv (ethanol): λ max nm (log ϵ) 366 (4.05).

Anal. Calcd. for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.36; N, 13.95. Found: C, 63.67; H, 6.36; N, 13.95.

Reaction of **11** with Ethanol.

A solution of 2.99 g (0.01 mole) of **11** in 100 ml of ethanol was refluxed for 10 days. After removal of the solvent by evaporation, the residue was recrystallized from ethyl acetate to give 1.30 g (38%) of ethyl 3-acetyl-8-cyano-1,4-dihydro-6,7-dimethyl-4-ethoxymethylpyrrolo[1,2-*a*]pyrimidine-4-carboxylate (**14**) as colorless needles, mp 223-224°; ir: ν cm^{-1} 2200 (CN), 1740 (CO); pmr: δ 0.91 (3H, t, J = 7 Hz, OCH_2CH_3), 1.20 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.0 (6H, s, 2 × CH_3), 2.24 (3H, s, $COCH_3$), 3.0-3.40 (2H, m, OCH_2CH_3), 3.85 (2H, s, CH_2), 4.16 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 7.65 (1H, bd, J = 6 Hz, C(2)-H), 10.91 (1H, bd, J = 6 Hz, NH); uv

(ethanol): λ max nm (log ε) 353 (3.95).

Anal. Calcd. for $C_{16}H_{23}N_3O_4$: C, 62.59; H, 6.71; N, 12.17. Found: C, 62.35; H, 6.81; N, 12.03.

The filtrate was concentrated *in vacuo* and the residue was subjected to silica gel short column chromatography. Elution with benzene gave 235 mg (7%) of ethyl 3-acetyl-9-cyano-4,5-dihydro-7,8-dimethyl-5-ethoxy-1*H*-pyrrolo[1,2-*a*][1,3]diazepine-5-carboxylate (**14**) as pale yellow needles, mp 174-176°; ir: ν cm^{-1} 2220 (CN), 1750 (CO); pmr: δ 1.0-1.21 (6H, m, $CO_2CH_2CH_3$ and OCH_2CH_3), 1.96 (6H, s, 2 × CH_3), 2.88 (1H, d, J = 15 Hz, C(4)-H), 3.35 (1H, d, J = 15 Hz, C(4)-H), 2.88-3.67 (2H, m, OCH_2CH_3), 4.08 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 7.33 (1H, s, C(2)-H), 9.72 (1H, bs, NH); uv (ethanol): λ max nm (log ε) 364 (4.11).

Anal. Calcd. for $C_{18}H_{23}N_3O_4$: C, 62.59; H, 6.71; N, 12.17. Found: C, 62.74; H, 6.92; N, 12.44.

Ethyl 9-Cyano-1,3-diacetyl-4,5-dihydro-7,8-dimethyl-1*H*-pyrrolo[1,2-*a*]-[1,3]diazepine-5-carboxylate (**16**).

A solution of 301 mg (1 mmole) of **14** in 5 ml of acetic anhydride and two drops of pyridine was heated at 80° for 6 hours. After removal of an excess acetic anhydride by evaporation, the residue was recrystallized from ethanol to give 195 mg (57%) of **17** as pale yellow needles, mp 139-141°; ir: ν cm^{-1} 2200 (CN), 1750, 1705 and 1660 (CO); pmr: δ 1.12 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$), 2.09 (3H, s, $NCOCH_3$), 2.21 and 2.25 (each 3H, each s, 2 × CH_3), 2.35 (3H, s, $COCH_3$), 4.03-4.25 (2H, m, $CO_2CH_2CH_3$), 3.25 (1H, d of d, J = 4, 18 Hz, C(4)-H), 5.56 (1H, t, J = 4 Hz, C(5)-H), 8.02 (1H, s, C(2)-H). One C(4)-proton could not be judged overlapped with methyl protons signals.

Anal. Calcd. for $C_{18}H_{21}N_3O_4$: C, 62.96; H, 6.16; N, 12.24. Found: C, 63.25; H, 6.12; N, 12.01.

4-Acetyl-1-(3-cyano-4,5-dimethyl-2-yl)pyrrole-2-carboxylic Acid (**18**).

Method a.

A solution of potassium hydroxide (1.2 mmoles) in 2 ml of water was added to a solution of 299 mg (1 mmole) of **11** in 50 ml of ethanol under ice cooling, and then the mixture was allowed to stand for 1 hour. After removal of the solvent by evaporation, the residue was dissolved in 5 ml of water. The aqueous solution was acidified by the addition of diluted hydrochloric acid under ice cooling. The resulting precipitate was collected and recrystallized from diluted ethanol to give 217 mg (80%) of **18** as colorless needles, mp 255-258°; ir: ν cm^{-1} 2200 (CN), 1690 (CO); pmr: δ 2.05 and 2.13 (each 3H, each s, 2 × CH_3), 2.41 (3H, s, $COCH_3$), 2.41 (3H, s, $COCH_3$), 3.0-3.65 (1H, bs, COOH), 7.27 (1H, d, J = 3 Hz, C(4)-H), 7.98 (1H, d, J = 3 Hz, C(5)-H).

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.98; H, 4.83; N, 15.49.Found: C, 62.10; H, 4.72; N, 15.47.

Method b.

A solution of sodium ethoxide (1.2 mmoles) in 5 ml of dry ethanol was added to a solution of 299 mg (1 mmole) of **11** under ice cooling, and then the mixture was allowed to stand for 0.5 hours. After removal of the solvent by evaporation, the residue was recrystallized from ethyl acetate-*n*-hexane to give 161 mg (55%) of sodium 3-acetyl-7-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]pyrrolo[1,2-*a*]pyrimidine-3a-carboxylate (**19**) as a pale yellow powder, mp 218-225°; ir: ν cm^{-1} 2220 (CN), 1710 (CO); pmr: δ 0.72 and 2.65 (each 1H, and d, J = 6 Hz, CH_2), 2.04 and 2.17 (each 3H, each s, 2 × CH_3), 2.23 (3H, s, $COCH_3$), 7.68 (1H, s, C(2)-H). A solution of 293 mg (1 mmole) of **19** dissolved in 5 ml of water was then acidified by the addition of diluted hydrochloric acid under ice cooling. The pecipitate was collected and recrystallized from ethanol to give 235 mg (87%) of **18**, which was identical with an authentic sample in all aspects.

Reaction of **7b** with Diazomethane.

Compound **7b** (3.15 g, 0.01 mole) was added to 200 ml of an ethereal solution containing excess diazomethane, and the suspension was stirred at 25° for 3 hours after which it was homogeneous. After standing in a refrigerator overnight, the resulting precipitate was collected and recrystallized from ethyl acetate to give 386 mg (10%) of diethyl 6-cyano-7,8-dimethyl-3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-1*H*-pyrazolo[3,4-*e*]pyrrolo[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**21**) as colorless needles, mp 151-152°; ir: ν cm^{-1} 2220 (CN), 1710 (CO); pmr (deuteriochloroform): δ 1.17-1.40 (6H, m, 2 × $CO_2CH_2CH_3$), 2.0 (6H, s, 2 × CH_3), 2.52 and 2.73 (each 1H, each d, J = 4 and 5 Hz, CH_2 on the aziridine ring), 4.04 (1H, d of d, J = 4, 5 Hz, C(3b)-H), 4.07-4.35 (4H, m, 2 × $CO_2CH_2CH_3$), 5.31 and 5.57 (each 1H, each d, J = 18 Hz, CH_2 on pyrazoline ring).

Anal. Calcd. for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 58.40; H, 5.71; N, 18.49.

The filtrate was concentrated *in vacuo*, and the residue was extracted with a hot mixture of ethyl acetate and *n*-hexane (1:1), from which 1.33 g (40%) of diethyl 7-cyano-2a,3a-dihydro-5,6-dimethyl-3*H*-cyclopropa[*e*]pyrrolo[1,2-*a*]pyrimidine-2a,3a-dicarboxylate (**20**) as pale yellow needles, mp 103-104°; ir: ν cm^{-1} 2220 (CN), 1760 (CO); pmr: δ 1.10-1.60 (6H, m, 2 × $CO_2CH_2CH_3$), 1.51 and 2.67 (each 1H, each d, J = 6 Hz, CH_2 on aziridine ring), 2.05 and 2.10 (each 3H, each s, 2 × CH_3), 4.05-4.30 (4H, m, 2 × $CO_2CH_2CH_3$), 8.06 (1H, s, C(2)-H).

Anal. Calcd. for $C_{17}H_{19}N_3O_4$: C, 61.99; H, 5.82; N, 12.76. Found: C, 62.14; H, 5.89; N, 12.78.

The insoluble solid in a mixture of ethyl acetate and *n*-hexane was recrystallized from ethanol to give 688 mg (19%) of diethyl 6-cyano-7,8-dimethyl-3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-3*H*-pyrazolo[3,4-*e*]pyrolo-[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**22**) as colorless needles of mp 139-140°; ir: ν cm^{-1} 2200 (CN), 1750 (CO); pmr: δ 1.20-1.44 (6H, m, 2 × $CO_2CH_2CH_3$), 1.95 and 2.0 (each 3H, each s, 2 × CH_3), 2.53 and 2.64 (each 1H, each d, J = 4 and 5 Hz, CH_2 on aziridine ring), 3.03 (1H, d of d, J = 4, 5 Hz, C(3b)-H), 4.05-4.43 (4H, m, 2 × $CO_2CH_2CH_3$), 6.70 (1H, s, NH), 6.98 (1H, s, =CH).

Anal. Calcd. for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 58.31; H, 5.67; N, 18.57.

Treatment of **21** with Acetic Anhydride.

A solution of 37 mg (0.1 mmole) of **21** in 2 ml of acetic anhydride and a drop of pyridine was heated at 60° for 3 hours. After removal of an excess acetic anhydride by evaporation, the residual oil was subjected to silica gel column chromatography. Elution with chloroform gave 8 mg of **22**, which was identical with an authentic sample in all aspects.

Diethyl 9-Cyano-4,5-dihydro-7,8-dimethyl-1*H*-pyrrolo[1,2-*a*][1,3]diazepine-3,5-dicarboxylate (**23**).

A solution of 329 mg (1 mmole) of **20** in 100 ml of ethanol was shaken with hydrogen over 200 mg of 5% palladium-carbon for 14 hours using a Skita apparatus. The reaction mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from ethyl acetate to give 122 mg (27%) of **23** as colorless needles, mp 183-185°; ir: ν cm^{-1} 2200 (CN), 1745 and 1690 (CO); pmr (deuteriochloroform): δ 1.12-1.36 (6H, m, 2 × $CO_2CH_2CH_3$), 2.05 (6H, s, 2 × CH_3), 2.68 (1H, d of d, J = 3, 21 Hz, C(4)-H), 3.74)1H, d of d, J = 6, 21 Hz, C(4)-H), 4.0-4.28 (4H, m, 2 × $CO_2CH_2CH_3$), 5.05 (1h, d of d, J = 3, 6 Hz, C(5)-H), 7.30 (1H, bs, C(2)-H).

Anal. Calcd. for $C_{17}H_{21}N_3O_4$: C, 61.62; H, 6.39; N, 12.68. Found: C, 61.57; H, 6.38; N, 12.75.

7-Cyano-2a,3a-dihydro-5,6-dimethyl-2a-ethoxycarbonyl-3*H*-cyclopropa-[*e*]pyrrolo[1,2-*a*]pyrimidine-3a-carboxylic Acid (**24**).

A solution of potassium hydroxide (1.2 mmoles) in 2 ml of water was added to a solution of 329 mg (1 mmole) of **20** in 50 ml of ethanol under ice cooling, and then the mixture was allowed to stand for 8 hours. After removal of the solvent by evaporation, the residue was dissolved in 5 ml of water. The aqueous solution was acidified by the addition of diluted hydrochloric acid under ice cooling. The precipitate was collected and recrystallized from ethyl acetate-*n*-hexane to give 295 mg (98%) of **24** as colorless needles, mp 172-173°; ir: ν cm^{-1} 2220 (CN), 1740 (CO); pmr (deuteriochloroform): δ 1.06 and 2.77 (each 1H, each d, J = 6 Hz, CH_2), 1.30 (3H, t, J = 7 Hz, $CO_2CH_2CH_3$),. 8.05 (1H, s, C(2)-H), 9.80 (1H, s, COOH).

Anal. Calcd. for $C_{15}H_{15}N_3O_4$: C, 59.79; H, 5.02; N, 13.95. Found: C, 59.85; H, 5.07; N, 13.70.

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