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# Synthesis and Reactions of Ethyl 6-Acetyl-2,3-diphenylimidazo[1,2-*a*] pyrimidine-5-carboxylate and Related Compounds[1)]

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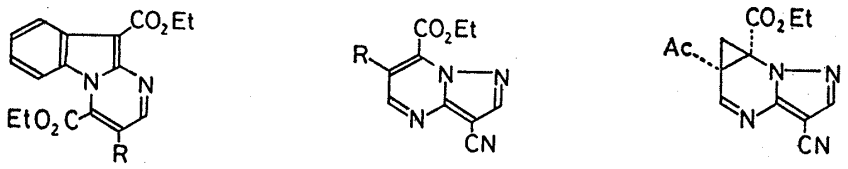
The reactions of the 6-acetyl-5-ethoxycarbonyl- or 5,6-diethoxycarbonylimidazo-[1,2-*a*]pyrimidine derivatives (**7a, b**), which were prepared by condensation of 2-amino-4,5-diphenylimidazole (**4**) with ethyl 3-ethoxymethylene-2,4-dioxovalerate (**5a**) or ethyl ethoxymethyleneoxaloacetate (**5b**), with diazomethane are described. Thus, reaction of **7a** with diazomethane at room temperature afforded three products whose structures were assigned as ethyl 5a-acetyl-4a,5a-dihydro-2,3-diphenyl-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]-pyrimidine-4a-carboxylate (**9**), ethyl 5a-acetyl-2,3-diphenyl-4a,5a,5b,7-tetrahydro-6*H*-aziridino[*c*]-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (**10**), and the 6-methyl analog (**11**) of **9**. When reacted with diazomethane under ice cooling, **7a** afforded only **9** in 73.0% yield. Reaction of **7b** with diazomethane at room temperature gave four products whose structures were assigned as diethyl 4a,5a-dihydro-2,3-diphenyl-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a,5a-dicarboxylate (**14**), diethyl 2,3-diphenyl-4a,5a,5b,7-tetrahydro-6*H*-aziridino[*c*]-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a,5a-dicarboxylate (**15**), diethyl 7,8-diphenyl-3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-3*H*-pyrazolo-[3,4-*e*]imidazo[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**16**), and diethyl 3a,9a-dihydro-7,8-diphenyl-4-methyl-3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**17**).

The chemical properties of **9** were also investigated. For example, **9** reacted with hydrochloric acid to give the 5,8-dihydro-5-chloromethylimidazo[1,2-*a*]pyrimidine (**19**) in excellent yield. When heated with acetic acid, **9** yielded the 5,8-dihydro-5-acetoxymethyl-imidazo[1,2-*a*]pyrimidine (**25**) in 12.7% yield, in addition to 40.0% yield of the 5-acetoxy-5,6-dihydro-9*H*-imidazo[1,2-*a*][1,3]diazepine (**26**), which was transformed into the *N*-imidazolylpyridone (**27**) by treatment with potassium hydroxide. On catalytic hydrogenation over 5% palladium charcoal, **9** gave the 5,6-dihydro-9*H*-imidazo[1,2-*a*][1,3]-diazepine (**32**), which was then derived to the 9*H*-imidazo[1,2-*a*][1,3]diazepine (**36**) by bromination followed by dehydrobromination.

**Keywords**——imidazo[1,2-*a*]pyrimidine; 5*H*-cyclopropa[e]imidazo[1,2-*a*]pyrimidine; aziridine; 3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine; ring expansion; ring transformation; 9*H*-imidazo[1,2-*a*][1,3]diazepine; 1-(imidazol-2-yl)pyridone; DBU; NBS

In the previous reports,[2)] we have shown that the catalytic hydrogenation or nucleophilic substitution of condensed pyrimidines having two carbonyl functional groups, such as pyrimido[1,2-*a*] indoles (**1**) and pyrazole[1,5-*a*]pyrimidines (**2**), occurred on the pyrimidine ring in a 1,4-fashion. Furthermore, compounds **1** and **2** have been shown to react with diazomethane giving the condensed cyclopropapyrimidine derivatives. Among them, the 6*H*-cyclopropa[*e*] pyrazolo[1,5-*a*]pyrimidine derivative (**3**) was used in a novel ring transformation as well as in ring expansion reactions to other heterocycles.[3)] We were interested in further exploring an analogous reaction of condensed pyrimidines, and the present paper describes the results of an investigation of imidazo[1,2-*a*]pyrimidine derivatives.

Imidazo[1,2-*a*]pyrimidines have generally been prepared by ring closure of 2-aminoimidazoles with $\beta$-dicarbonyl compounds or 2-aminopyrimidines with $\alpha$-halo ketones.[4)] Murmann *et al.*[5)] reported the synthesis and reactions of some derivatives of imidazo[1,2-*a*]pyrimidine with analgesic, antiinflammatory, antipyretic, and anticonvulsant activities. Pyl[6)] also reported the synthesis, and nucleophilic and electrophilic substitutions of the 7-methyl-2-phenylimidazo[1,2-*a*] pyrimidine derivatives. Previously, we reported[7)] the condensation of 2-aminobenzimidazole with ethyl 3-ethoxymethylene-2,4-dioxovalerate (**5a**) or ethyl ethoxymethyleneoxaloacetate (**5b**) to afford 3-acetyl-4-ethoxycarbonyl- or 3,4-diethoxycarbonyl-

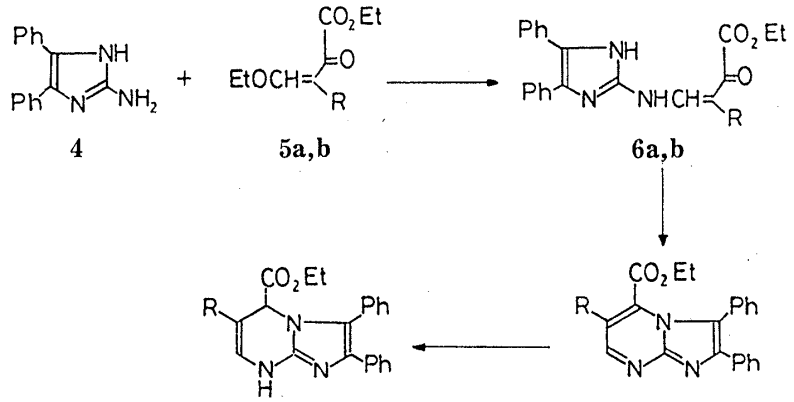


1 2 3

R=Ac or $CO_2Et$

Chart 1

imidazo[1,2-*a*] pyrimidines in moderate yields. Reaction of **5a,b** with 2-aminoimidazole, however, resulted in the formation of a complex mixture from which no products could be isolated. Meanwhile, satisfactory results were obtained when **5a, b** were treated with 2-amino-4,5-diphenylimidazole (**4**).[8] Thus, reaction of **4** with **5a, b** in ethanol under ice cooling afforded the 2-imidazolylaminomethylene derivatives (**6a, b**) ,which were subsequently cyclized without difficulty by refluxing **6a** in ethanol or by heating **6b** over its melting point to give good yields of the desired imidazo[1,2-*a*]pyrimidines (**7a, b**). The analytical and spectral data were consistent with the structures **7a, b.** Catalytic hydrogenation of **7a, b** in methanol over 5% palladium charcoal (Pd-C) afforded the 5,8-dihydropyrimidines (**8a, b**) in 60—70% yields, and this is in fair agreement with the results for **1** and **2**.[2]



4 5a,b 6a,b 8a,b 7a,b

a : R=Ac b : R=$CO_2Et$

Chart 2

Treatment of **7a** with an excess of diazomethane at room temperature gave three products, pale yellow needles of mp 193—195°C ($C_{24}H_{21}N_3O_3$) (**9**), colorless needles of mp 165—167°C ($C_{25}H_{23}N_3O_3$) (**10**), and pale yellow needles of mp 182—183°C ($C_{25}H_{23}N_3O_3$) (**11**), in yields of 5, 35.9 and 25.2%, respectively. The minor products (**9** and **11**) were shown to have a 5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine moiety on the basis of the proton magnetic resonance (PMR) spectra (detailed in the experimental section), which are similar to those of the 6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]pyrimidines (**3**).[2] The structure of the main product (**10**) was presumed to be ethyl 5a-acetyl-2,3-diphenyl-4a,5a,5b,7-tetrahydro-6*H*-aziridino[*c*]-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate from its PMR spectrum, which exhibited signals due to the cyclopropane ring protons at 1.16 and 2.83 ppm as a doublet with a coupling constant ($J$) of 6 Hz, aziridine ring methylene protons at 1.61 and 2.70 ppm as a doublet with $J$=5 Hz, and an aziridine ring methine proton at 4.30 ppm as a triplet with $J$=5 Hz.[2] The stereochemistry of **10** was chemically confirmed by the following experiments. On catalytic hydrogenation in the presence of 5% Pd–C, **10** was transformed into the 6-methyl-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine (**12**), mp 239—240°C, by the hydrogeno-

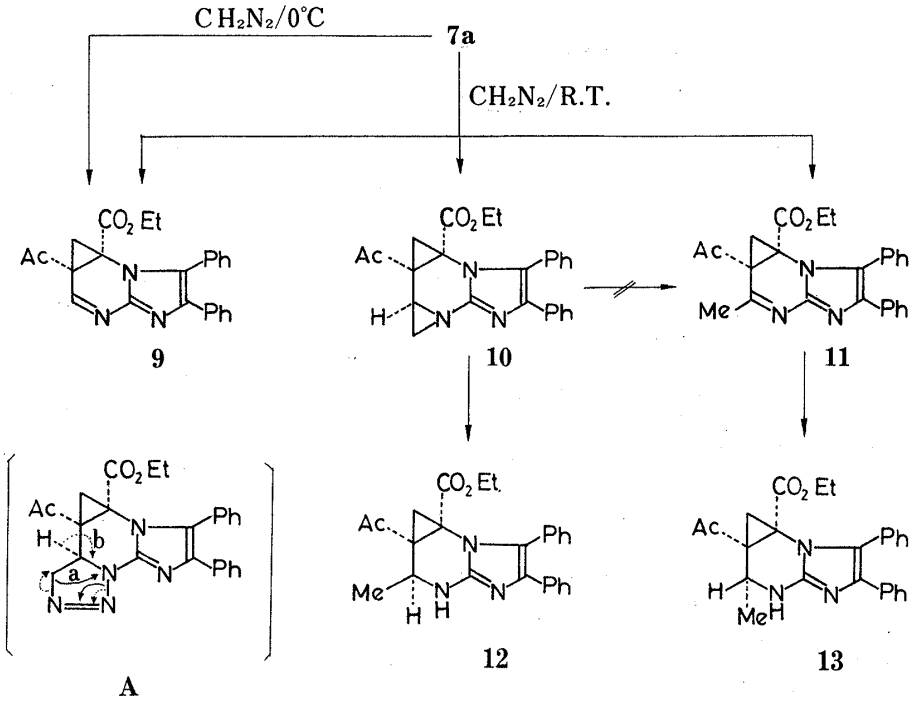



Chart 3

lysis of the aziridine ring of **10** in good yield. Catalytic hydrogenation of **11** with platinum oxide ($PtO_2$) gave its dihydro derivative (**13**), mp 192—193°C in 43.5% yield. They were found to be configurational isomers with respect to the C(6)-methyl group from their PMR spectra. In the PMR spectra (DMSO-$d_6$), the C(6)-proton of **12** (multiplet at 4.30 ppm which collapsed into a quartet on deuterium exchange) and the C(6)-methyl protons of **13** (doublet at 1.33 ppm) appeared at lower field than that of **13** (quartet at 3.60 ppm) and those of **12** (doublet at 1.12 ppm), respectively, due to the anisotropic effect of the acetyl group located on the same side.

In addition, it should be mentioned that the formation of **10** and **11** can be reasonably interpreted on the basis of the formation of an unstable pyrazoline (A)[9] followed by conversion *via* path a) to **10** and *via* path b) to **11**, because pyrolysis of **10** to **11** resulted in recovery of the starting material. On the other hand, when **7a** reacted with diazomethane under ice cooling, only compound **9** was obtained in 73.0% yield.

Next, reaction of **7b** with an excess of diazomethane at room temperature gave four products, pale yellow needles of mp 154—155°C ($C_{25}H_{23}N_3O_4$) (**14**), colorless needles of mp 161—162°C ($C_{26}H_{25}N_3O_4$) (**15**), cololress needles of mp 190—192°C ($C_{26}H_{25}N_5O_4$) (**16**), and pale yellow needles of mp 184—185°C ($C_{26}H_{25}N_5O_4$) (**17**), in yields of 7.7, 30.0, 18.8 and 15.3%, respectively. The structural assignments of **14** and **15** were readily made on the

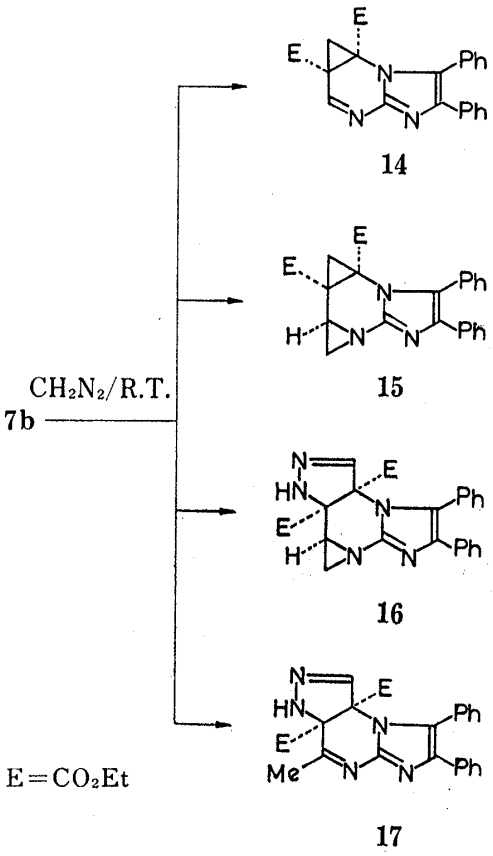



Chart 4

basis of the results of elemental analysis and by comparison of their spectral data with those of **9** and **10**, respectively.

The infrared (IR) spectra (KBr) of **16** and **17** exhibited strong bands at 3275 and 3235 $cm^{-1}$, respectively, due to the NH group. The PMR spectra of **16** showed characteristic signals due to azididine ring protons [2.56 and 3.01 ppm (each 1H, each d, $J$=5 Hz), and 3.08 ppm (1H, t, $J$=5 Hz)], although **17** showed a methyl signal at 2.26 ppm instead of the signals of aziridine ring protons. Based on the analytical and spectral data described above, the 3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine and the 3a,9a-dihydro-4-methyl-3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine structure were assigned to the products **16** and **17**. The compound **17** did not, however, react like **7a** to yield **14** in good yield even under mild conditions. Our interest was, then focussed on an investigation of the chemical properties of **9**.

When refluxed in methanol for 2 h, **9** reacted like **3** and formed a methanol adduct (**18**) in 69.6% yield. The stereochemistry was determined by comparison of the C(6)-proton signal [as a doublet ($J$=4 Hz) coupled with the NH group which collapsed into a singlet on deuterium exchange] with that of **12** [as a multiplet which collapsed into a quartet on deuterium exchange] in their PMR spectra. Treatment of **9** with concentrated hydrochloric acid in dioxane gave the 5-chloromethyl-5,8-dihydroimidazo[1,2-*a*]pyrimidine (**19**) in excellent yield. The elemental analysis, mass spectrum (MS) $m/z$: 435 ($M^+$), and PMR spectrum [4.0 ppm (2H, s, $CH_2Cl$)] were consistent with this structure. Acetylation of **19** with acetic anhydride and pyridine yielded a monoacetate (**20**), whose PMR spectrum showed a signal due to a C(7)-proton at 8.73 ppm shifted downfield by 0.75 ppm relative to that of **19** (7.98 ppm) by the anisotropic effect of the N(8)-acetyl group. The same compound was obtained independently by treatment of **18** with hydrochloric acid. Analogously, treatment of **9** with 48% hydrobromic acid in dioxane gave **21** with an empirical formula $C_{24}H_{23}Br_2N_3O_3$ in 65.0% yield. Stirring with silicic acid in chloroform, **21** was transformed into the 5-bromomethyl-5,8-dihydroimidazo [1,2-*a*]pyrimidine (**22**), which proved **21** to be ethyl 6-acetyl-8a-bromo-5-bromomethyl-2,3-

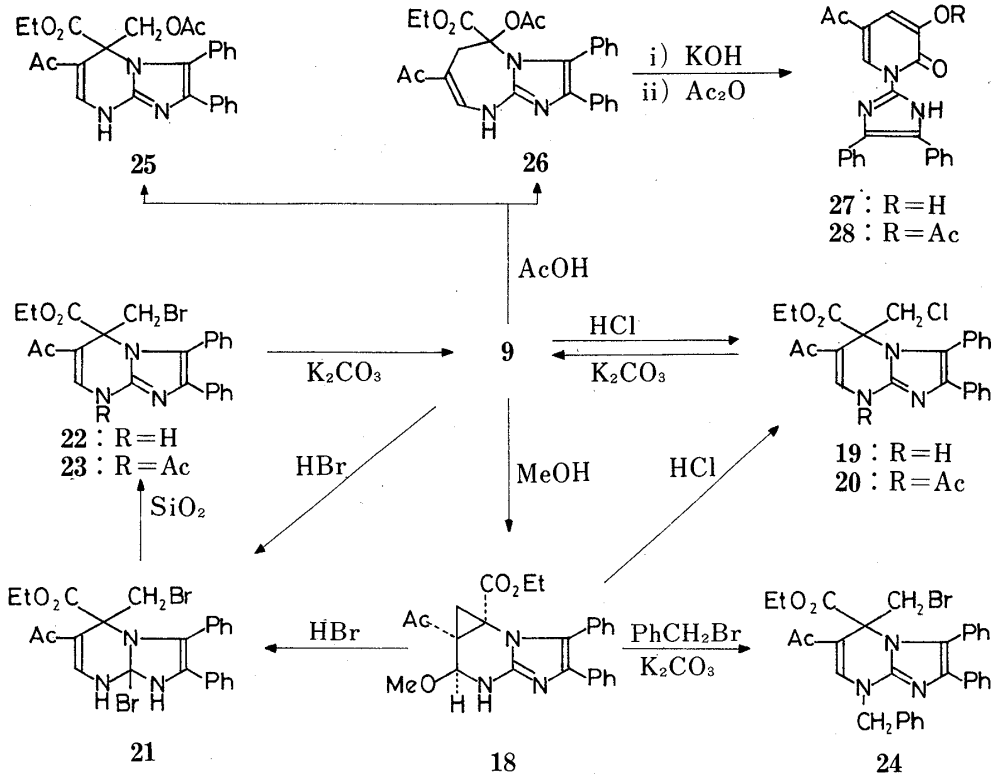



Chart 5

diphenyl-1,5,8,8a-tetrahydroimidazo[1,2-*a*]pyrimidine-5-carboxylate. In addition, treatment of **21** with acetic anhydride and pyridine at room temperature afforded the N(8)-acetate, whose PMR spectrum {8.70 ppm [1H, s, C(7)–H]} is consistent with the structure **23**. These halomethyl derivatives (**19** and **22**) were converted to **9** by refluxing them with potassium carbonate in acetone. Although a 8-benzyl-5-bromomethyl-5,8-dihydroimidazo[1,2-*a*]pyrimidine (**24**) was not isolated in the reaction of **9** with benzyl bromide, the compound **24** was prepared alternatively from **18** and benzyl bromide in the presence of portassium carbonate in low yield. When heated with acetic acid, **9** afforded ethyl 5-acetoxymethyl-6-acetyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (**25**) in 12.7% yield in addition to 40.0% yield of ethyl 5-acetoxy-7-acetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*] [1,3]-diazepine-5-carboxylate (**26**). The elemental analysis and PMR spectra [4.43 ppm (2H, q, $J$=12 Hz, $CH_2OCOCH_3$) in **25** and 3.51 ppm (2H, bs, $CH_2$) in **26**] were consistent with these structures. In order to confirm the structural assignment, **26** was treated with ethanolic potassium hydroxide to give 5-acetyl-3-hydroxy-1-(4,5-diphenylimidazol-2-yl)-2-pyridone (**27**), whose PMR spectrum showed signals at 7.20 and 8.37 ppm as two sets of doublets ($J$=3 Hz), which clearly indicate the presence of a 2-pyridone moiety.[10] The product gave a dark brown color with $FeCl_3$–$K_3[Fe(CN)_6]$ in ethanol and gave the monoacetate (**28**) on reaction with acetic anhydride and pyridine under ordinary conditions. The transformation of **26** to **27** presumably proceeds in the same way as that of ethyl 8-acetoxy-6-acetyl-3-cyano-7,8-dihydro-4*H*-pyrazolo[1,5-*a*][1,3]diazepine-8-carboxylate to the *N*-pyrazolylpyridone, shown in the previous paper.[10]

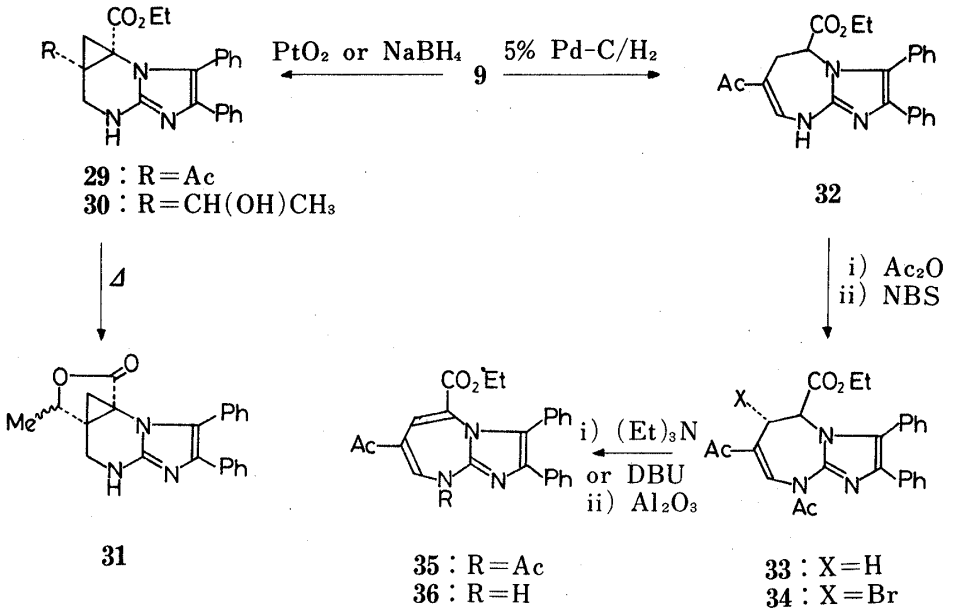



Chart 6

Next, the reduction of **9** was investigated. On catalytic hydrogenation in the presence of $PtO_2$ under atmospheric pressure, **9** was transformed into its dihydro derivative (**29**), mp 247—249°C, in 73.0% yield. The PMR spectrum of **29** showed signals due to cyclopropane ring protons at 1.92 and 2.36 ppm as a doublet ($J$=6 Hz), respectively. Reduction of **9** with sodium borohydride in ethanol gave the dihydro alcohol (**30**), which was then simply refluxed in xylene to give the bicyclo lactone (**31**), whose IR spectrum shows a characteristic band at 1790 $cm^{-1}$ due to a lactone carbonyl group. On the other hand, when hydrogenated over 5% Pd–C using a Skita apparatus, **9** was transformed into ethyl 7-acetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (**32**), mp 216—218°C, in 66.3% yield. The PMR spectrum of **32** showed signals of a characteristic ABX pattern due to a >CH–$CH_2$-

group [2.45 ppm (1H, dd, $J$=15 and 3 Hz), 3.90 (1H, dd, $J$=15 and 6 Hz), and 4.90 (1H, dd, $J$=6 and 3 Hz)] in addition to a broad singlet at 6.76 ppm which collapsed into a singlet on deuterium exchange.

Though a few derivatives of 1*H*-imidazo[1,2-*a*][1,3]diazepine,[11] some of which have anticonvulsant and hypoglycemic activities, have been reported, 9*H*-imidazo[1,2-*a*][1,3]-diazepine has not hitherto been reported. An attempt to prepare ethyl 7-acetyl-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (**36**) from **32** by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation was unsuccessful, only a tarry mixture being obtained.[12] Thus, **32** was treated with acetic anhydride and pyridine to give the acetate (**33**), which was then brominated with N-bromosuccinimide (NBS) in carbon tetrachloride in the presence of benzoyl peroxide to afford the 6-bromo-9-acetyl-5,6-dihydro-9*H*-imidazo[1,2-*a*][1,3]diazepine derivative (**34**) in quantitative yield. Since the PMR spectrum of **34** revealed the C(5)- and C(6)-protons as two sets of doublets ($J$=5 Hz)[13] at 4.97 and 5.81 ppm, the stereostructure of **34** was assigned as *trans*. Treatment of **34** with triethylamine in refluxing benzene afforded the 9-acetyl-9*H*-imidazo[1,2-*a*][1,3]diazepine (**35**) as a pale yellow powder, mp 206—208°C, in 47.3% yield. Dehydrobromination of **34** with 1,5-diazabicyclo[5,4,0]undec-5-ene (DBU)[14] was achieved more successfully to give **35** in 72.9% yield. Compound **35**, upon treatment with basic alumina in refluxing benzene, underwent hydrolysis of the *N*-acetyl group to give **36** as a red powder, mp 303—305°C, in 30.7% yield. The structural determinations of **35** and **36** were based on the results of elemental analysis and their spectral data detailed in the experimental section.

## Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were recorded on a JASCO model IRA-1 spectrophotometer and the UV spectra on a JASCO UVIDEC-505 spectrophotometer. The PMR spectra were taken at 90 MHz with a Hitachi R-24A spectrometer and chemical shifts are expressed in ppm downfield from TMS as an internal standard. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and b=broad. The MS were recorded with a Hitachi RMU-7L spectrometer.

**Ethyl 3-(4,5-Diphenyl-2-imidazolylamino)methylene-2,4-dioxovalerate (6a) and Ethyl 4,5-Diphenyl-2-imidazolylaminomethyleneoxaloacetate (6b)**——A solution of 0.01 mol of **5a** (or **5b**) in 5 ml of EtOH was added to a stirred solution of 0.01 mol of 4,5-diphenyl-2-aminoimidazole (**4**) in 50 ml of EtOH with cooling in an ice-bath. After stirring had been continued for 2 h, the yellow precipitate was collected by filtration, washed with cold EtOH, and dried. These products were found to exist as mixtures of unseparable geometrical isomers as judged from their PMR spectra, and to have one molecule of ethanol of crystallization as judged from the elemental analysis data.

**6a**; Yellow powder of mp 124—125°C. Yield: 95.8%. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3600—2600 (NH), 1750 and 1640 (CO). PMR (DMSO-$d_6$) $\delta$: 0.91—1.30 (6H, m, 2×$CH_2C\underline{H}_3$), 2.20 and 2.40 (each s, $COCH_3$), 3.20—3.80 and 4.10—4.40 (each m, 2×$C\underline{H}_2CH_3$), 7.0—7.70 (10H, m, Ar–H), 7.87 and 8.80 (each bs, CH). *Anal.* Calcd for $C_{23}H_{21}N_3O_4\cdot C_2H_5OH$: C, 66.80; H, 6.05; N, 9.35. Found: C, 66.57; H, 5.82; N, 9.33.

**6b**; Yellow powder of mp 108—110°C. Yield: 80.7%. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400—2600 (NH), 1740, 1700 and 1640 (CO). PMR (DMSO-$d_6$) $\delta$: 0.80—1.40 (9H, m, 3×$CH_2C\underline{H}_3$), 3.20—4.40 (6H, m, 3×$C\underline{H}_2CH_3$), 7.0—7.60 (10H, m, Ar–H), 8.81 (1H, bs, CH). *Anal.* Calcd for $C_{24}H_{23}N_3O_5\cdot C_2H_5OH$: C, 65.12; H, 6.10; N, 8.76. Found: C, 64.95; H, 5.99; N, 8.97.

**Ethyl 6-Acetyl-2,3-diphenylimidazo[1,2-a]pyrimidine-5-carboxylate (7a)**——A solution of 4.49 g (0.01 mol) of **6a** in 200 ml of EtOH was refluxed for 2 h. After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give 3.19 g (86.4%) of **7a** as yellow needles of mp 226—227°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1750 and 1690 (CO). PMR (DMSO-$d_6$) $\delta$: 1.09 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.70 (3H, s, $COCH_3$), 3.49 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 7.20—7.70 (10H, m, Ar–H), 9.25 [1H, s, C(7)–H]. *Anal.* Calcd for $C_{23}H_{19}N_3O_3$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.46; H, 5.08; N, 10.63.

**Diethyl 2,3-Diphenylimidazo[1,2-a]pyrimidine-5,6-dicarboxylate (7b)**——Compound **6b** (4.79 g, 0.01 mol) was heated at 130—150°C in an oil bath for 20 min, then cooled. The residue was recrystallized from EtOH to give 3.94 g (94.8%) of **7b** as yellow needles of mp 180—181°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1750 and 1730 (CO). PMR (DMSO-$d_6$) $\delta$: 1.09 and 1.28 (each 3H, each t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.47 and 4.30 (each 2H, each q, $J$=7 Hz, 2×$CO_2C\underline{H}_2CH_3$), 7.10—7.70 (10H, m, Ar–H), 8.95 [1H, s, C(7)–H]. *Anal.* Calcd for $C_{24}H_{21}N_3O_5$: C, 69.38; H, 5.10; N, 10.12. Found: C, 69.29; H, 5.09; N, 10.23.

**Ethyl 6-Acetyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (8a) and Diethyl 5,8-Dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5,6-dicarboxylate (8b)**——A solution of 0.01 mol of **7a** (or **7b**) in 200 ml of MeOH was shaken with $H_2$ over 1.5 g of 5% Pd-C for 15 h using a Skita apparatus. The reaction mixture was filtered and concentrated *in vacuo* to give **8a** (or **8b**), which was recrystallized from EtOH.

**8a**; Colorless plates of mp 224—226°C. Yield: 64.4%. IR $\nu_{max}^{KBr}$: 3200—2400 (NH), 1740 and 1640 (CO), 1590 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.83 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.21 (3H, s, $COCH_3$), 3.50—3.90 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.55 [1H, s, C(5)–H], 7.10—7.60 (10H, m, Ar–H), 7.85 [1H, s, C(7)–H], 11.10 (1H, bs, NH). *Anal.* Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.40; N, 10.85. Found: C, 71.46; H, 5.60; N, 11.04.

**8b**; Colorless plates of mp 198—200°C. Yield: 72.4%. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2400 (NH), 1770 and 1730 (CO), 1620 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.86 and 1.17 (each 3H, each t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 3.50—4.30 (4H, m, 2×$CO_2C\underline{H}_2CH_3$), 5.48 [1H, s, C(5)–H], 7.10—7.60 [11H, m, Ar–H and C(7)–H], 10.95 (1H, bs, NH). *Anal.* Calcd for $C_{24}H_{23}N_3O_4$: C, 69.05; H, 5.55; N, 10.07. Found: C, 69.18; H, 5.75; N, 10.32.

**Ethyl 5a-Acetyl-4a,5a-dihydro-2,3-diphenyl-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (9)**——Compound **7a** (3.85 g, 0.01 mol) was added to 200 ml of an ethereal solution containing excess diazomethane (prepared from 21 g of *N*-nitrosomethylurea[14]) with cooling in an ice bath, and the suspension was stirred for 10 h. The precipitate was collected and recrystallized from benzene–ligroin to give 2.90 g (73.0%) of **9** as pale yellow needles of mp 193—195°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1750 and 1720 (CO). PMR (DMSO-$d_6$) $\delta$: 0.85 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.85 and 2.75 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.40 (3H, s, $COCH_3$), 3.20—3.70 (2H, m, $CO_2C\underline{H}_2CH_3$), 7.10—7.60 (10H, m, Ar–H), 8.61 [1H, s, C(6)–H]. *Anal.* Calcd for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.03; H, 5.55; N, 10.49.

**Reaction of 7a with Diazomethane at Room Temperature**——Compound **7a** (1 g, 2.6 mmol) was added to 100 ml of an ethereal solution containing excess diazomethane, and the suspension was stirred for 2 d at room temperature. The precipitate was collected and subjected to silica gel column chromatography. Elution with 16.7% AcOEt in $CHCl_3$ gave first 270 mg (25.2%) of ethyl 5a-acetyl-4a,5a-dihydro-2,3-diphenyl-6-methyl-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (**11**) as pale yellow needles of mp 182—183°C (from benzene–ligroin). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740 and 1700 (CO), 1610 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.82 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.85 and 2.75 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.26 and 2.35 (each 3H, each s, $CH_3$ and/or $COCH_3$), 3.20—3.80 (2H, m, $CO_2C\underline{H}_2CH_3$), 7.10—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{25}H_{23}N_3O_3$: C, 72.62; H, 5.61; N, 10.16. Found: C, 72.71; H, 5.81; N, 10.39. The second elution, with the same solvent, gave 52 mg (5.0%) of **9**. Ethyl 5a-Acetyl-2,3-diphenyl-4a,5a,5b,7-tetrahydro-6*H*-aziridino[*c*]-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (**10**) was eluted later with the same solvent as colorless needles of mp 165—167°C (from benzene), 385 mg (35.9%). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740 and 1710 (CO). PMR ($CDCl_3$) $\delta$: 0.93 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.16 and 2.83 (each 1H, each d, $J$=6 Hz, $CH_2$ of cyclopropane ring), 1.61 and 2.70 (each 1H, each d, $J$=5 Hz, $CH_2$ of aziridine ring), 2.36 (3H, s, $COCH_3$), 3.40 (1H, t, $J$=5 Hz, CH of aziridine ring), 3.50—3.80 (2H, m, $CO_2C\underline{H}_2CH_3$), 7.10—7.70 (10H, m, Ar–H). *Anal.* Calcd for $C_{25}H_{23}N_3O_3$: C, 72.62; H, 5.61; N, 10.16. Found: C, 72.83; H, 5.55; N, 10.35.

**Ethyl (4a*R**,5a*S**,6*S**)-5a-Acetyl-2,3-diphenyl-6-methyl-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo-[1,2-*a*]pyrimidine-4a-carboxylate (12)**——A solution of 413 mg (1 mmol) of **10** in 200 ml of EtOH was shaken with $H_2$ over 140 mg of 5% Pd-C for 5 h using a Skita apparatus. The reaction mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from EtOH to give 354 mg (87.0%) of **12** as colorless needles of mp 239—240°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2800 (NH), 1730 and 1700 (CO). PMR (DMSO-$d_6$) $\delta$: 0.82 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.12 (3H, d, $J$=6 Hz, $CHC\underline{H}_3$), 1.95 and 2.26 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.20 (3H, s, $COCH_3$), 3.55 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.30 (1H, m, CH), 6.90—7.50 (10H, m, Ar–H). *Anal.* Calcd for $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.07; N, 10.23. Found: C, 71.99; H, 6.08; N, 10.23.

**Ethyl (4a*R**,5a*S**,6*R**)-5a-Acetyl-2,3-diphenyl-6-methyl-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo-[1,2-*a*]pyrimidine-4a-carboxylate (13)**——A solution of 413 mg (1 mmol) of **11** in 200 ml of EtOH was shaken with $H_2$ over 130 mg of $PtO_2$ for 5 h under atmospheric pressure. The reaction mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from EtOH to give 104 mg (25%) of **13** as colorless needles of mp 192—193°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2800 (NH), 1730 and 1720 (CO). PMR (DMSO-$d_6$) $\delta$: 0.80 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.33 (3H, d, $J$=6 Hz, $CHC\underline{H}_3$), 1.95 and 2.30 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.10 (3H, s, $COCH_3$), 3.20—3.50 (2H, m, $CO_2C\underline{H}_2CH_3$), 3.60 (1H, q, $J$=6 Hz, CH), 7.0—7.50 (10H, m, Ar–H). *Anal.* Calcd for $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.07; N, 10.11. Found: C, 72.56; H, 5.89; N, 10.04.

**Reaction of 7b with Diazomethane at Room Temperature**——Compound **7b** (4.15 g, 0.01 mol) was added to 200 ml of an ethereal solution containing excess diazomethane, and the suspension was stirred for 3 d at room temperature. The precipitate was collected and subjected to silica gel column chromatography. Elution with 12.5% AcOEt in $CHCl_3$ gave first 721 mg (15.3%) of diethyl 3a,9a-dihydro-7,8-diphenyl-4-methyl-3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**17**) as colorless needles of mp 184—185°C (from benzene). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3235 (NH), 1760 (CO). PMR ($CDCl_3$) $\delta$: 1.20 and 1.28 (each 3H, each t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 2.26 (3H, s, $CH_3$), 3.90—4.50 (4H, m, 2×$CO_2C\underline{H}_2CH_3$), 6.12 (1H, s, N=CH), 6.82 (1H, s, NH), 7.0—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{26}H_{25}N_5O_4$: C, 66.23; H, 5.34; N, 14.85. Found: C, 66.14; H, 5.27; N, 14.86. The second elution with same solvent gave 1.33 g (30.0%) of diethyl 2,3-diphenyl-4a,5a,5b,7-tetrahydro-6*H*-aziridino[*c*]-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a,5a-dicarboxylate (**15**) as colorless needles of mp 161—162°C (benzene–ligroin). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740

(CO). PMR ($CDCl_3$) $\delta$: 0.93 (6H, t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 1.20 and 2.81 (each 1H, each d, $J$=6 Hz, $CH_2$ on cyclopropane ring), 1.57 and 2.65 (each 1H, each d, $J$=5 Hz, $CH_2$ on aziridine ring), 3.20—3.80 [3H, m, $CO_2C\underline{H}_2CH_3$ and C(5b)–H], 4.17 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 7.0—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{26}H_{25}N_3O_4$: C, 70.41; H, 5.68; N, 9.48. Found: C, 70.63; H, 5.55; N, 9.49. Diethyl 7,8-diphenyl-3a,3b,5,9a-tetrahydro-4*H*-aziridino[*c*]-3*H*-pyrazolo[3,4-*e*]imidazo[1,2-*a*]pyrimidine-3a,9a-dicarboxylate (**16**) was eluted later with the same solvent as colorless needles of mp 190—192°C (from benzene), 886 mg (18.8%). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3275 (NH), 1760 and 1750 (CO). PMR ($CDCl_3$) $\delta$: 1.23 and 1.27 (each 3H, each t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 2.56 and 3.01 (each 1H, each d, $J$=5 Hz, $CH_2$ on aziridine ring), 3.08 [1H, t, $J$=5 Hz, C(2b)–H], 3.90—4.50 (4H, m, 2×$CO_2CH_2C\underline{H}_3$), 5.90 (1H, s, N=CH), 6.73 (1H, s, NH), 7.0—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{26}H_{25}N_5O_4$: C, 66.23; H, 5.34; N, 14.85. Found: C, 66.16; H, 5.27; N, 14.91. The residual oil, which was obtained by evaporation of ether, was chromatographed on silica gel. Elut on with $CHCl_3$ gave 330 mg (7.7%) of diethyl 4a,5a-dihydro-2,3-diphenyl-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]-pyrimidine-4a,5a-dicarboxylate (**14**) as pale yellow needles of mp 154—155°C (from ligroin). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1750 (CO). PMR (DMSO-$d_6$) $\delta$: 0.85 and 1.15 (each 3H, each t, $J$=7 Hz, 2×$CO_2CH_2C\underline{H}_3$), 1.95 and 2.86 (each 1H, each d, $J$=6 Hz, $CH_2$), 3.45 and 4.12 (each 2H, each q, $J$=7 Hz, 2×$CO_2C\underline{H}_2CH_3$), 7.10—7.60 (10H, m, Ar–H), 8.40 [1H, s, C(6)–H]. *Anal.* Calcd for $C_{25}H_{23}N_3O_4$: C, 69.91; H, 5.40; N, 9.79. Found: C, 69.92; H, 5.54; N, 9.86.

**Ethyl (4a*R**,5a*R**,6*S**)-5a-Acetyl-2,3-diphenyl-6-methoxy-4a,5a,6,7-tetrahydro-5*H*-cylropropa[*e*]-imidazo[1,2-*a*]pyrimidine-4a-carboxylate (18)**——A solution of 3.99 g (0.01 mol) of **9** in 200 ml of MeOH was refluxed for 2 h. After removal of the solvent by evaporation, the residue was recrystallized from MeOH to give 3.0 g (69.6%) of **18** as colorless needles of mp 195—197°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3220—2800 (NH), 1740 and 1720 (CO). PMR (DMSO-$d_6$) $\delta$: 0.80 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.90 and 2.30 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.22 (3H, s, $COCH_3$), 3.25 (3H, s, $OCH_3$), 3.40—3.80 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.15 [1H, d, $J$=4 Hz, C(6)–H], 7.0—7.50 (10H, m, Ar–H), 8.18 (1H, d, $J$=4 Hz, NH). *Anal.* Calcd for $C_{25}H_{25}N_3O_4$: C, 69.59; H, 5.84; N, 9.74. Found: C, 69.37; H, 5.73; N, 9.80.

**Ethyl 6-Acetyl-5-chloromethyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (19)**——a): A solution of 399 mg (1 mmol) of **9** and 5 ml of conc. HCl in 50 ml of dioxane was refluxed for 5 h. After removal of the solvent by evaporation, the residue was recrystallized from AcOEt–*n*-hexane to give 413 mg (94.7%) of **19** as colorless needles of mp 234—236°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3100—2500 (NH), 1750 and 1640 (CO), 1590 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.93 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.22 (3H, s, $COCH_3$), 3.50—4.20 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 4.0 (2H, s, $CH_2$), 7.0—7.70 (10H, m, Ar–H), 7.98 [1H, s, C(7)–H]. 11.20 (1H, bs, NH). MS *m/z*: 435 ($M^+$). *Anal.* Calcd for $C_{24}H_{22}ClN_3O_3$: C, 66.13; H, 5.09; N, 9.64. Found: C, 66.40; H, 5.15; N, 9.57.

b): A solution of 413 mg (1 mmol) of **18** and 5 ml of conc. HCl in 50 ml of EtOH was refluxed for 24 h. After removal of the solvent by evaporation, the residue was recrystallized from AcOEt–*n*-hexane to give 205 mg (47.1%) of **19**, which was identified by mixed melting point determination and IR comparison with an authentic sample.

**Ethyl 5-Chloromethyl-6,8-diacetyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (20)**——A solution of 435 mg (1 mmol) of **19** in 5 ml of acetic anhydride and two drops of pyridine was allowed to stand overnight. The resulting precipitate was collected and recrystallized from AcOEt–*n*-hexane to give 372 mg (77.9%) of **20** as colorless needles of mp 195—197°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1750, 1730 and 1640 (CO). PMR (DMSO-$d_6$) $\delta$: 0.97 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.43 and 3.07 (each 3H, each s, 2×$COCH_3$), 3.80 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 4.10 (2H, q, $J$=12 Hz, $CH_2$), 7.10—7.60 (10H, m, Ar–H), 8.73 [1H, s, C(7)–H]. *Anal.* Calcd for $C_{26}H_{24}ClN_3O_4$: C, 65.34; H, 5.06; N, 8.79. Found: C, 65.50; H, 5.06; N, 8.77.

**Ethyl 5-Bromomethyl-6,8-diacetyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (23)**——A solution of 280 mg (0.5 mmol) of **21** in 5 ml of acetic anhydride and two drops of pyridine was allowed to stand for 3 h. The resulting precipitate was collected and recrystallized from EtOH to give 219 mg (84.0%) of **23** as colorless needles of mp 185—188°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1750, 1730 and 1640 (CO). PMR (DMSO-$d_6$) $\delta$: 0.95 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.40 and 3.05 (each 3H, each s, 2×$COCH_3$), 3.70 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 3.95 (2H, q, $J$=12 Hz, $CH_2$), 7.10—7.60 (10H, m, Ar–H), 8.70 [1H, s, C(7)–H]. *Anal.* Calcd for $C_{26}H_{24}BrN_3O_4$: C, 59.78; H, 4.63; N, 8.04. Found: C, 59.74; H, 4.61; N, 7.90.

**Ethyl 6-Acetyl-8a-bromo-5-bromomethyl-2,3-diphenyl-1,5,8,8a-tetrahydroimidazo[1,2-*a*]pyrimidine-5-carboxylate (21)**——a): A solution of 399 mg (1 mmol) of **9** and 1 ml of 48% HBr in 50 ml of dioxane was refluxed for 3 h. After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give 367 mg (65.3%) of **21** as colorless needles of mp 221—223°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400—2500 (NH), 1740 and 1670 (CO), 1600 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.95 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.24 (3H, s, $COCH_3$), 3.40—4.0 (2H, m, $CO_2C\underline{H}_2CH_3$), 3.93 (2H, s, $CH_2$), 5.90 (2H, bs, 2×NH), 7.0—7.80 (10H, m, Ar–H), 8.0 [1H, s, C(7)–H]. *Anal.* Calcd for $C_{24}H_{23}Br_2N_3O_3$: C, 51.35; H, 4.13; N, 7.49. Found: C, 51.57; H, 4.33; N, 7.54.

b): From 431 mg (1 mmol) of **18** and 1 ml of 48% HBr in EtOH, 508 mg (90.5%) of **21**, which was identical with an authentic sample was obtained by the method described above.

**Ethyl 6-Acetyl-5-bromomethyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (22)**——A suspension of 561 mg (1 mmol) of **21** and 1 g of $SiO_2$ in 50 ml of $CHCl_3$ was stirred vigorously for 24 h at room temperature. After $SiO_2$ had been filtered off, the filtrate was concentrated *in vacuo*. The residue

was recrystallized from dil. EtOH to give 392 mg (81.6%) of **22** as colorless needles of 215—217°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400—2400 (NH), 1740 and 1640 (CO), 1600 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.96 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.22 (3H, s, $COCH_3$), 3.50—4.10 (2H, m, $CO_2C\underline{H}_2CH_3$), 3.95 (2H, bs, $CH_2$), 7.0—7.70 (10H, m, Ar–H), 7.98 [1H, s, C(7)–H], 11.40 (1H, bs, NH). *Anal.* Calcd for $C_{24}H_{22}BrN_3O_3$: C, 60.01; H, 4.62; N, 8.75. Found: C, 60.30; H, 4.50; N, 8.94.

**Ethyl 6-Acetyl-8-benzyl-5-bromomethyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (24)**——Potassium carbonate (0.5 g) was added to a solution of 431 mg (1 mmol) of **18** and 0.5 ml of benzyl bromide in 50 ml of acetone, and the mixture was refluxed for 64 h. After the insoluble solid had been filtered off, the filtrate was concentrated *in vacuo* to give an oily material, which was chromatographed on silica gel. Elution with $CHCl_3$ gave 53 mg (9.2%) of **24** as colorless needles of mp 205—206°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740 and 1630 (CO), 1600 (C=C). PMR (DMSO-$d_6$) $\delta$: 1.0 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.13 (3H, s, $COCH_3$), 3.40—4.20 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.0 (2H, s, $CH_2Br$), 5.22 (2H, q, $J$=15 Hz, $NCH_2$), 7.0—7.60 [11H, m, Ar–H and C(7)–H]. *Anal.* Calcd for $C_{31}H_{28}BrN_3O_3$: C, 65.26; H, 4.95; N, 7.37. Found: C, 65.53; H, 4.87; N, 7.42.

**Ethyl 5-Acetoxymethyl-6-acetyl-5,8-dihydro-2,3-diphenylimidazo[1,2-*a*]pyrimidine-5-carboxylate (25) and Ethyl 5-Acetoxy-7-acetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (26)**——A solution of 3.99 g (0.01 mol) of **9** in 100 ml of AcOH was refluxed for 4 h. After removal of the solvent by evaporation, the residue was subjected to silica gel column chromatography. Elution with $CHCl_3$ gave first 1.84 g (40.0%) of **26** as colorless needles of mp 226—228°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2600 (NH), 1750 (CO), 1600 (C=C). PMR (DMSO-$d_6$) $\delta$: 1.07 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.59 (3H, s, $OCOCH_3$), 2.20 (3H, s, $COCH_3$), 3.51 (2H, bs, $CH_2$), 3.86 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 7.0—7.50 [11H, m, Ar–H and C(8)–H], 10.52 (1H, bs, NH). *Anal.* Calcd for $C_{26}H_{25}N_3O_5$: C, 67.96; H, 5.48; N, 9.15. Found: C, 67.70; H, 5.57; N, 9.30. Compound **25** was eluted later with 50% AcOEt in $CHCl_3$ as colorless needles of mp 235—238°C (from EtOH), 0.58 g (12.7%). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2600 (NH), 1740 and 1640 (CO), 1590 (C=C). PMR (DMSO-$d_6$) $\delta$: 0.93 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.92 (3H, s, $OCOCH_3$), 2.18 (3H, s, $COCH_3$), 3.20—4.0 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.43 (2H, q, $J$=12 Hz, $CH_2$), 7.0—7.60 (10H, m, Ar–H), 7.92 [1H, s, C(7)–H], 11.10 (1H, bs, NH). *Anal.* Calcd for $C_{26}H_{25}N_3O_5$: C, 67.96; H, 5.48; N, 9.15. Found: C, 67.72; H, 5.41; N, 9.13.

**5-Acetyl-3-hydroxy-1-(4,5-diphenylimidazol-2-yl)-2-pyridone (27)**——A solution of 48 mg (1.2 mmol) of NaOH in 3 ml of $H_2O$ was added to a solution of 459 mg (1 mmol) of **26** in 100 ml of EtOH, and the mixture was then refluxed for 30 min. After removal of the solvent by evaporation, the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with water, dried ($Na_2SO_4$), and concentrated. The residue was recrystallized from benzene to give 224 mg (60.4%) of **27** as colorless needles of mp 207—209°C. $FeCl_3$–$K_3$[Fe(CN)$_6$] test: positive (dark brown). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3340 (OH and NH), 1640 (CO). PMR (DMSO-$d_6$) $\delta$: 2.47 (3H, s, $COCH_3$), 7.20 [1H, d, $J$=3 Hz, C(4)–H], 7.20—7.60 (10H, m, Ar–H), 8.37 [1H, d, $J$=3 Hz, C(6)–H], 10.0 and 13.10 (each 1H, each bs, NH and/or OH). *Anal.* Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.32. Found: C, 70.89; H, 4.75; N, 11.28.

**3-Acetoxy-5-acetyl-1-(4,5-diphenylimidazol-2-yl)-2-pyridone (28)**——A solution of 371 mg (1 mmol) of **27** in 5 ml of acetic anhydride and two drops of pyridine was allowed to stand for 3 h. The resulting precipitate was collected and recrystallized from benzene to give 227 mg (55.0%) of **28** as colorless plates of mp 209—211°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3320 (NH), 1780 and 1670 (CO). PMR (DMSO-$d_6$) $\delta$: 2.31 and 2.53 (each 3H, each s, 2×$COCH_3$), 7.20—7.60 (10H, m, Ar–H), 7.85 [1H, d, $J$=3 Hz, C(4)–H], 8.79 [1H, d, $J$=3 Hz, C(6)–H], 13.20 (1H, bs, NH). *Anal.* Calcd for $C_{24}H_{19}N_3O_4$: C, 69.72; H, 4.63; N, 10.16. Found: C, 69.47; H, 4.63; N, 10.20.

**Reaction of 19 (or 22) with Potassium Carbonate**——A suspension of 1 mmol of **19** (or **22**) and 0.5 g of $K_2CO_3$ in 100 ml of acetone was refluxed for 2 h. After the insoluble solid had been filtered off, the filtrate was condensed *in vacuo*. The residue was recrystallized from benzene–ligroin to give **9** (50—60% yield), which was identical with an authentic sample.

**Ethyl 5a-Acetyl-2,3-diphenyl-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (29)**——A solution of 399 mg (1 mmol) of **9** in 50 ml of dioxane was shaken with $H_2$ over 130 mg of $PtO_2$ under atmospheric pressure. The reaction mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from $CH_3CN$ to give 293 mg (73.0%) of **29** as colorless needles of mp 247—249°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2800 (NH), 1730 and 1700 (CO). PMR (DMSO-$d_6$) $\delta$: 0.80 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.92 and 2.36 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.20 (3H, s, $COCH_3$), 3.11 [1H, d, $J$=14 Hz, C(6)–H], 3.40—3.80 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.10 [1H, dd, $J$=14 and 3 Hz, C(6)–H], 7.02 (1H, d, $J$=3 Hz, NH), 7.10—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.78; N, 10.47. Found: C, 71.88; H, 5.92; N, 10.36.

**Ethyl 2,3-Diphenyl-5a-(1-hydroxyethyl-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylate (30)**——$NaBH_4$ (91 mg, 2.4 mmol) was added to a solution of 399 mg (1 mmol) of **9** in 50 ml of EtOH, and then the mixture was stirred for 1 h. Excess $NaBH_4$ was decomposed by the addition of AcOH, then the solvent was removed by evaporation. The residue was extracted with $CHCl_3$, and the $CHCl_3$ extract was washed with water, and dried ($Na_2SO_4$). After removal of the solvent by evaporation, the residue was recrystallized from EtOH to give 217 mg (53.9%) of **30** as colorless needles of mp 245—247°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3520 and 3280 (NH and/or OH), 1710 (CO). PMR (DMSO-$d_6$) $\delta$: 0.84 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.16 (3H, d, $J$=7 Hz, $CHC\underline{H}_3$), 1.51 and 1.61 (each 1H, each d, $J$=6 Hz, $CH_2$), 2.92 [1H, d, $J$=12 Hz, C(6)–H], 3.20—3.70 (3H, m, $CO_2C\underline{H}_2CH_3$ and $C\underline{H}OH$), 3.91 [1H, bd, $J$=12 Hz, C(6)–H], 4.59 (1H, d,

$J$=5 Hz, OH), 6.57 (1H, bs, NH), 7.0—7.60 (10H, m, Ar–H). *Anal.* Calcd for $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.42. Found: C, 71.56; H, 6.30; N, 10.40.

**2,3-Diphenyl-5a-(1-hydroxyethyl)-4a,5a,6,7-tetrahydro-5*H*-cyclopropa[*e*]imidazo[1,2-*a*]pyrimidine-4a-carboxylic Acid Lactone (31)**——A solution of 403 mg (1 mmol) of **30** in 100 ml of xylene was refluxed for 20 h, then cooled. The precipitate was collected and recrystallized from MeOH to give 304 mg (85.3%) of **31** as colorless needles of mp>300°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400—2800 (NH), 1790 (CO). PMR (DMSO-$d_6$) $\delta$: 1.51 (3H, d, $J$=6 Hz, $CHC\underline{H}_3$), 1.87 and 2.26 (each 1H, each d, $J$=6 Hz, $CH_2$), 3.10 [1H, d, $J$=13 Hz, C(6)–H], 3.95 [1H, bd, $J$=13 Hz, C(6)–H], 4.65 (1H, q, $J$=6 Hz, $C\underline{H}CH_3$), 6.71 (1H, bs, NH), 7.0—7.50 (10H, m, Ar–H). *Anal.* Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 74.14; H, 5.48; N, 11.53.

**Ethyl 7-Acetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (32)**——A solution of 399 mg (1 mmol) of **9** in 100 ml of THF was shaken with $H_2$ over 5% Pd-C for 6 h under atmospheric pressure. The reaction mixture was filtered and concentrated *in vacuo*. The residue was recrystallized from EtOH to give 266 mg (66.3%) of **32** as colorless needles of mp 216—218°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2600 (NH), 1750 and 1610 (CO). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 248 (4.19), 332 (4.26). PMR ($CDCl_3$) $\delta$: 1.13 (3H, t, $J$= 7 Hz, $CO_2CH_2\underline{C}H_3$), 1.78 (3H, s, $COCH_3$), 2.45 [1H, dd, $J$=15 and 3 Hz, C(6)–H], 3.90 [1H, dd, $J$=15 and 6 Hz, C(6)–H], 3.90—4.30 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.90 [1H, dd, $J$=6 and 3 Hz, C(5)–H], 6.76 [1H, bs, C(8)-H], 7.10—7.50 (10H, m, Ar–H), 12.55 (1H, bs, NH). *Anal.* Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.78; N, 10.47. Found: C, 72.08; H, 5.71; N, 10.51.

**Ethyl 7,9-Diacetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (33)**——A solution of 401 mg (1 mmol) of **32** in 10 ml of acetic anhydride and three drops of pyridine was allowed to stand overnight. After removal of excess acetic anhydride by evaporation, the residue was recrystallized from ligroin to give 256 mg (57.8%) of **33** as colorless needles of mp 152—160°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1750, 1700 and 1660 (CO). PMR (DMSO-$d_6$) $\delta$: 1.11 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.38 and 2.43 (each 3H, each s, 2×$COCH_3$), 2.60 [1H, bd, $J$=16 Hz, C(6)–H], 3.30 [1H, dd, $J$=16 and 3 Hz, C(6)–H], 3.90—4.40 (2H, m, $CO_2C\underline{H}_2CH_3$), 5.10 [1H, t, $J$=3 Hz, C(5)–H], 7.10—7.70 (10H, m, Ar–H), 8.28 (1H, bs, NH). *Anal.* Calcd for $C_{26}H_{25}N_3O_4$: C, 70.41; H, 5.68; N, 9.48. Found: C, 70.20; H, 5.53; N, 9.72.

**Ethyl (5*R**,6*S**)-6-Bromo-7,9-diacetyl-5,6-dihydro-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (34)**——A solution of 443 mg (1 mmol) of **33** and 214 mg (1.2 mmol) of NBS in 100 ml of $CCl_4$ in the presence of 10 mg of benzoyl peroxide was refluxed for 5 h, then cooled. The resulting precip.tate was filtered off, and the filtrate was condensed *in vacuo*. The residue was recrystallized from benzene–ligroin to give 522 mg (100%) of **34** as colorless needles of mp 150—154°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740, 1720 and 1660 (CO). PMR ($CDCl_3$) $\delta$: 1.20 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.43 and 2.58 (each 3H, each s, 2×$COCH_3$), 4.0—4.40 (2H, m, $CO_2C\underline{H}_2CH_3$), 4.97 [1H, d, $J$=5 Hz, C(6)–H], 5.81 [1H, d, $J$=5 Hz, C(5)–H], 7.10—7.60 (10H, m, Ar–H), 8.49 [1H, s, C(8)–H]. *Anal.* Calcd for $C_{26}H_{24}BrN_3O_4$: C, 59.78; H, 4.63; N, 8.04. Found: C, 59.54; H, 4.36; N, 8.25.

**Ethyl 7,9-Diacetyl-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (35)**——a) A solution of 522 mg (1 mmol) of **34** and 121 mg (1.2 mmol) of triethylamine in 100 ml of abs. benzene was refluxed for 3 h, then cooled. The resulting precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The residue was recrystallized from EtOH to give 209 mg (47.3%) of **35** as a pale yellow powder of mp 206—208°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1720, 1700, and 1680 (CO). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 238 (4.47), 278 (4.27), and 348 (3.16). PMR (DMSO-$d_6$) $\delta$: 0.96 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.48 and 2.50 (each 3H, each s, 2×$COCH_3$), 3.65 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 7.10—7.50 [11H, m, Ar–H and C(6)–H], 8.00 [1H, s, C(8)–H]. MS $m/z$: 441 ($M^+$). *Anal.* Calcd for $C_{26}H_{23}N_3O_4$: C, 70.73; H, 5.25; N, 9.52. Found: C, 70.46; H, 5.34; N, 9.52.

b) DBU (152 mg, 1 mmol) was added to a solution of 522 mg (1 mmol) of **34** in 100 ml of abs. benzene with stirring at room temperature. After stirring had been continued for 10 min, the resulting precipitate was filtered off and the filtrate was concentrated *in vacuo*. The residue was recrystallized from EtOH to give 372 mg (72.9%) of **35**, which was identified by mixed melting point determination and IR comparison with an authentic sample.

**Ethyl 7-Acetyl-2,3-diphenyl-9*H*-imidazo[1,2-*a*][1,3]diazepine-5-carboxylate (36)**——$Al_2O_3$ (1 g) was added to a solution of 441 mg (1 mmol) of **35** in 50 ml of abs. benzene, and the suspension was refluxed with stirring for 12 h. $Al_2O_3$ was filtered off, and the filtrate was concentrated *in vacuo*. The residue was recrystallized from $CH_3CN$ to give 123 mg (30.7%) of **36** as a red powder of mp 303—305°C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3200—2600 (NH), 1710 and 1750 (CO). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 248 (4.26), 292 (4.23), and 427 (2.97). PMR (DMSO-$d_6$) $\delta$: 0.84 (3H, t, $J$=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.55 (3H, s, $COCH_3$), 3.55 (2H, q, $J$=7 Hz, $CO_2C\underline{H}_2CH_3$), 6.92 [1H, s, C(6)–H], 7.00—7.60 [11H, m, Ar–H and C(8)–H]. MS $m/z$: 399 ($M^+$). *Anal.* Calcd for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.99; H, 5.31; N, 10.54.

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