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A Facile and Stereoselective Azepine-Ring Formation at the Periphery of Pyridone and Pyrido[1,2-*a*]pyrimidone Systems *via* Intramolecular Imine and Carbonyl Ene Reactions

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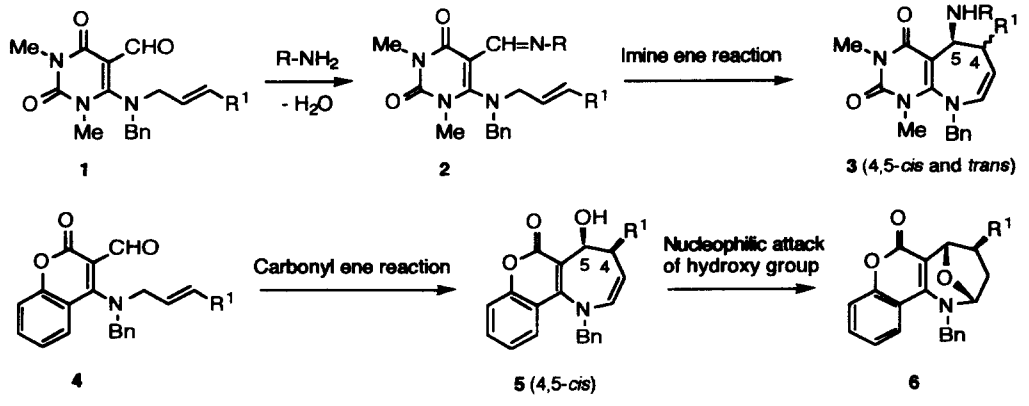
Abstract: Thermal reaction of the *N*-alkyl and *N*-aryl imines of 2-(alk-2-enylamino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9**) gave pyrido[1',2':1,2]pyrimido[4,5-*b*]azepines **11-14** in good to excellent yields. Similarly, the imines of 4-(alk-2-enylamino)-1,6-dimethyl-2-oxo-1*H*-pyridine 3-carboxaldehyde (**15**) afforded pyrido[4,3-*b*]azepines **16** and 2,4-ethanopyrido[4,3-*d*]pyrimidines **17** depending on the reaction conditions, the latter of which were secondary products from azepines **16**. Heating aldehyde **15** in appropriate solvents also gave 2,4-ethanopyrido[4,3-*d*][1,3]oxazine **18**. On the other hand, the thermal reaction of aldehyde **9** gave pyridopyrimidoazepine **20** and 12,13-ethanopyrido[1',2':1,2]pyrimido[5,4-*b*]azepine **21** in good total yields. These azepine-ring formation could be regarded as the intramolecular imine and carbonyl ene reactions at the periphery of the heterocyclic systems. Therein, the reactions proceeded in a highly stereoselective manner to give 4,5-*cis* azepines. The details and limitations of these ene reactions will be described.

Introduction

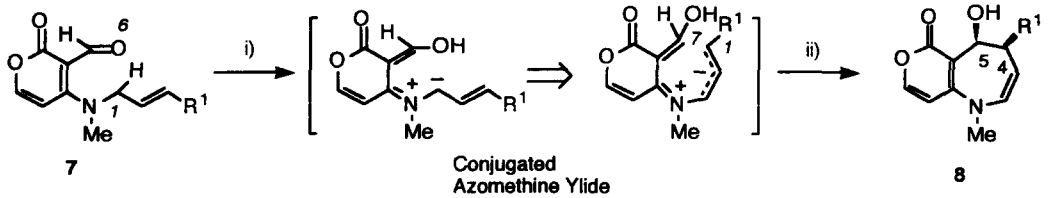
Recently, we have developed a new type of cyclization reaction at the periphery of pyrimidine and 1-benzopyran systems; heating the imines of 6-(alk-2-enylamino)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine 5-carboxaldehyde **2** in toluene gave pyrimido[4,5-*b*]azepine derivative **3** as a mixture of 4,5-*cis* and -*trans* azepines.[1] On the other hand, the thermal reaction of 4-(alk-2-enylamino)-2-oxo-1*H*-1-benzopyran carboxaldehyde **4** also gave 1-benzopyrano[3,4-*b*]azepine derivative **5** as a 4,5-*cis* isomer (Scheme 1).[2]

Scheme 1.



These azepine-ring formations could be regarded formally as the intramolecular imine and carbonyl ene reactions classified to Type III.[3] Since the examples of the Type III ene reaction were rarely found in literatures[4] and these ene reactions proceeded smoothly without catalysts,[5,6] our attention was focused on the reaction mechanism. Molecular orbital (MO) calculations using PM3 method were accomplished for the model reaction of 4-(*N*-allylmethylamino)-2-oxo-2*H*-pyran 3-carboxaldehyde (**7**: R^1= H) to 1-methyl-5-hydroxy-4,5-dihydropyrano[4,3-*b*]azepin-6(1*H*)-one (**8**: R^1= H) (Scheme 2). The results suggested that the azepine-ring formation was constituted of two consecutive orbital-controlled reactions; the [1,6] hydrogen shift leading to a conjugated azomethine ylide intermediate and its [1,7] electrocyclic ring-closure.[2] The latter step was concluded to be the rate-determining one.

Scheme 2.



7 8

Reactions: i) [1,6] Hydrogen shift (antarafacial); ii) [1,7] Electrocyclization (conrotatory)

Although the azepine-ring formation is much of interest because of its mechanistic novelty and synthetic utility, the generality and stereoselectivity of the ene reactions have not been established; neither the carbonyl ene reaction of aldehyde **1** took place under usual conditions nor the desired imines could be prepared by the reaction of aldehyde **4** with primary amines. Moreover, a mixture of 4,5-*cis* and -*trans* azepines was formed in the reaction of aldehyde **1** with primary amines.

In order to obtain better understandings on the azepine-ring formation, we examined the similar reaction of 4-(alk-2-enylamino)-2-oxo-1*H*-pyridoine 3-carboxaldehyde **9** and 2-(alk-2-enylamino)-3-oxo-4*H*-pyrido[1,2-*a*]-pyrimidine 3-carboxaldehyde **15**, which possess characteristic cross conjugated π-electron systems at the periphery of the heterocycles.

This paper describes a successful application of the azepine-ring formation to these systems through both imine and carbonyl ene reactions, which proceed under extremely mild conditions with a high stereoselectivity. The limitations of this azepine-ring formation will be discussed.

Imine Ene Reaction at the Periphery of Pyrido[1,2-*a*]pyrimidone and Pyridone Systems

The thermal reaction of 2-(*N*-allylbenzylamino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9a**) with aniline (**10a**) and isobutylamine (**10b**) was examined. In both cases, pyrido[1',2':1,2]pyrimido[4,5-*b*]azepines **11a** and **11b** were obtained in excellent yields. To complete the azepine-ring formation within limited periods of time, the reaction temperature above 80 °C (under reflux in benzene) was required. The reaction with aniline (**10a**) in refluxing benzene was slower than that with isobutylamine (**10b**). However, utilizing dehydrating reagent such as molecular sieves (4Å), or similar reaction at an elevated temperature gave substantially same results for the both amines.

Similar reactions of aldehydes **9b-d** with amines **10a-c** were examined under several conditions and the results are summarized in Table 1. Dihydroazepines **12-14** were obtained as single diastereomers in excellent yields and their structures were established by the analytical and spectroscopic data. The relative stereochemistry between the 4- and 5-positions in the azepine-ring of products **12-14** was deduced to be the same from the signal patterns of olefin protons at the 3-position (δ 4.50-5.22; double-double-doublet, *J*= *ca.* 2-3, 2-5, and 10 Hz) and was suggested to be *cis* as discussed in the previous paper.[1] Finally, the 4,5-*cis* configuration was unambiguously confirmed by X-ray crystal-structure analysis of dihydroazepine **12a** (Fig. 1).[7]

Scheme 3.

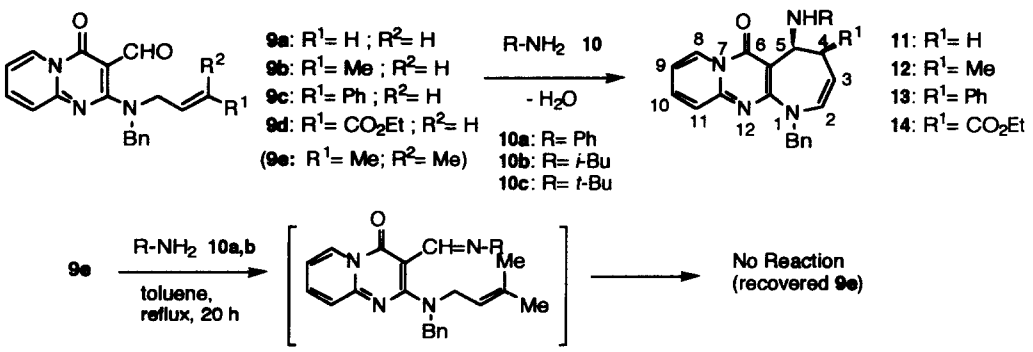


Table 1. Reaction of Aldehydes **9** with Primary Amines **10** Leading to Fused Azepine Derivatives **11-14**

Entry	Substrates	R^1	R^2	R	Solvent	Temp.	Time (h)	Yield (%)[a]
1	**9a** + **10a**	H	H	Ph	benzene	reflux	20	**11a**/97
2	**9a** + **10a**	H	H	Ph	toluene	reflux	4	**11a**/94
3	**9a** + **10b**	H	H	*i*-Bu	benzene	reflux	3	**11b**/94
4	**9a** + **10b**	H	H	*i*-Bu	toluene	reflux	2	**11b**/88
5	**9b** + **10a**	Me	H	Ph	benzene	reflux	20	**12a**/91
6	**9b** + **10b**	Me	H	*i*-Bu	benzene	reflux	4	**12b**/88
7	**9b** + **10c**	Me	H	*t*-Bu	benzene	r.t.[b]	60	**12c**/88
8	**9c** + **10a**	Ph	H	Ph	benzene	reflux	6	**13a**/88
9	**9c** + **10b**	Ph	H	*i*-Bu	benzene	reflux	4	**13b**/83
10	**9d** + **10a**	CO_2Et	H	Ph	benzene	r.t.[b]	45	**14a**/78
11	**9d** + **10a**	CO_2Et	H	Ph	benzene	reflux	10	**14a**/73[c]

a) Based on the isolated products. b) Molecular sieves (4Å) were used as dehydrating reagent.
c) Another product **21d**, a carbonyl ene type product, was also obtained in 22% yield.

4,5-*cis* Azepine **12c** was given in 88% yield by the reaction of aldehyde **9b** and *tert*-butylamine (**10c**) at room temperature (Entry 7), regardless of the bulkiness of the substituent on the imine nitrogen. The electron-withdrawing nature of alkenyl substituent (R^1) facilitated the rate of azepine-ring formation; the reaction of aldehyde **9d** with aniline (**10a**) at room temperature gave azepine **14a** in 78% yield (Entry 10). On the other hand, a similar reaction in benzene under reflux gave imine ene product **14a** and carbonyl ene product **21d** in 73 and 22% yields, respectively (Entry 11). Interestingly, the alkenyl substituent (R^2) with *Z*-configuration in the imine interferred the ene reaction; the reaction of aldehyde **9e** and amines **10a,b** in refluxing toluene gave the starting aldehyde **9e** as the hydrolyzed product of the corresponding imines.

Similarly, the 2-pyridone derivatives **15a,b**, bearing the same reactive functions in the 3- and 4-positions, were converted with primary amines **10a,b** in refluxing benzene to give dihydroazepines **16a-c**, which were converted to 2,4-ethanopyrido[4,3-*d*]pyrimidines **17a-c** during the purification procedures (Table 2). The transformation of **16** to **17** was easily explained; the amino nitrogen at the 5-position attacked nucleophilically to the 2-position in **16**.[1] The configuration of methyl group (R^1) at the 10-position in **17c** was deduced to be *exo* from the coupling constant between the 4- and 10-H (*J*= *ca.* 0 Hz). This reveals also the 4,5-*cis* selectivity in the azepine-ring formation. As mentioned above, the reaction of aldehydes **9** and **15** with primary amines **10** gave the azepines fused by heterocyclic systems. It should be also noted that these unactivated imines underwent under extremely mild conditions.[5c] 4,5-*cis* Azepines were exclusively formed from the imines of aldehydes

Scheme 4.

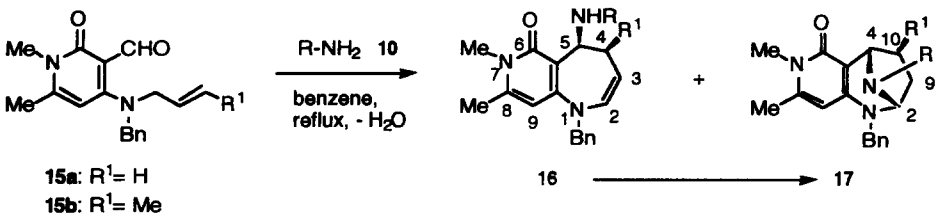


Table 2. Reaction of Aldehydes **15** with Primary Amines **10** Leading to Fused Azepine Derivatives **17**

Entry	Substrates	R^1	R	Time (h)	Ratio[a] of **16**:**17** in the crude products	Final Product/ Yield (%)[b]
1	**15a** + **10a**	H	Ph	2	17 : 83	**17a**/89
2	**15a** + **10b**	H	*i*-Bu	1	100 : 0	**17b**/93
3	**15b** + **10a**	Me	Ph	8	76 : 34	**17c**/90

a) The ratio was determined by ^{1}H NMR spectra of the crude products. b) Based on the isolated products.

bearing 3-substituted (alk-2-enyl)amino groups with *E*-configurations. It was suggested that the imine formation from aldehydes **9** and **15** and amines **10** might be a crucial step as well as 1,7-electrocyclic ring-closure of the azomethine ylide intermediates.

Carbonyl Ene Reaction at the Periphery of Pyrido[1,2-a]pyrimidone and Pyridone Systems

Next our concern was focused on the thermal behaviors of the aldehydes **9** and **15**. Aldehyde **15a** gave 2,4-ethanopyrido[4,3-*d*][1,3]oxazine **18a** and a fully conjugated pyrido[4,3-*b*]azepine **19** in 78 and 7% yields, respectively. A similar reaction of aldehydes **15b** and **15c** gave only **18b** and **18c** in excellent yields (Table 3). The structures of these products were determined also on the basis of the analytical and spectroscopic data by comparison with those of the related system reported.[2] To reduce the intricacies for the structural determination of [1,3]oxazine products, the X-ray crystal-structure analysis of **18c** was accomplished (Fig. 2).[7]

Scheme 5.

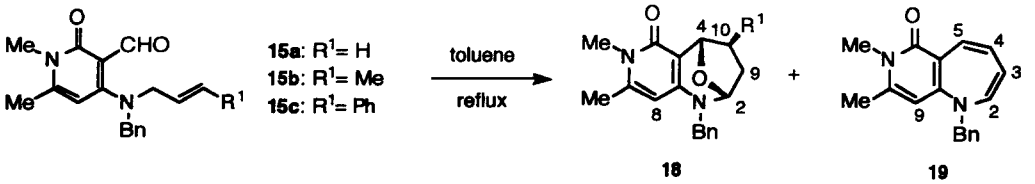


Table 3. Thermal Reaction of Aldehydes **15** Leading to Fused Azepine Derivatives **18** and **19**

Entry	Substrate	R^1	Time (h)	Products/Yield (%)[a]
1	**15a**	H	24	**18a**/78 **19**/7
2	**15b**	Me	80	**18b**/79[b]
3	**15c**	Ph	48	**18c**/80

a) Isolated yield. b) The starting material **15b** was recovered in 19% yield.

Heating aldehyde **9a** in refluxing xylene gave dihydroazepine **20a**, [1,3]oxazine **21a**, and a fully conjugated azepine **22**. Similar reactions of aldehydes **9b-e** were also examined (Table 4). More elevated reaction temperatures were required to complete the azepine-ring formation through the carbonyl ene reaction of aldehydes **9** than those of aldehydes **15**. The carbonyl ene reaction of aldehydes **9** and **15** proceeded more sluggishly than the corresponding imine ene reaction. An apparent effect of ethoxycarbonyl substituent in the alkenyl moiety on the reactivity was also observed; heating **9d** in toluene under reflux gave dihydroazepine **20d** and [1,3]oxazine **21d** in a quantitative total yield (Entry 4). The ene reaction of **9d** proceeded even in refluxing benezene to give **20d** in 68% yield. The alkenyl substituent R^2 also interferred the carbonyl ene reaction; heating the solution of aldehyde **9e** in xylene did not provide any changes. The effect of the substituent with *Z*-configuration in the alkene moiety on the azepine-ring formation will be discussed by the MO calculations utilizing PM3 method.[8]

Scheme 6.

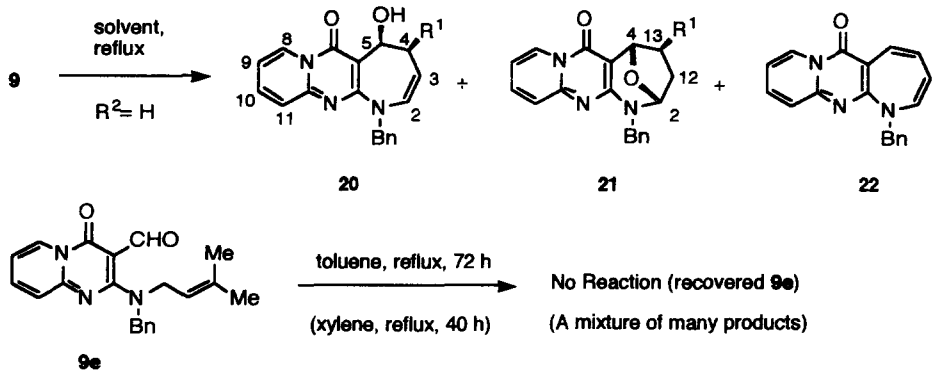


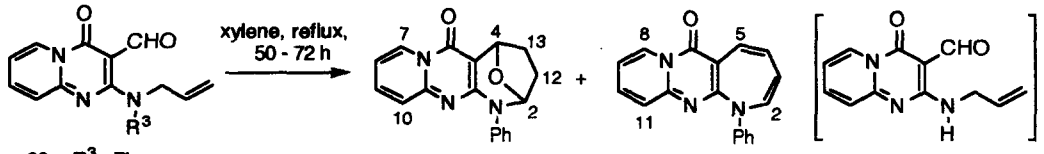
Table 4. Thermal Reaction of Aldehydes **9** Leading to Fused Azepine Derivatives **20**, **21**, and **22**.

Entry	Substrate	R^1	Solvent	Time (h)	Products/Yield (%)[a]
1	**9a**	H	xylene	20	**20a**/22 **21a**/33 **22**/42
2	**9b**	Me	xylene	60	**20b**/26 **21b**/36[b]
3	**9c**	Ph	xylene	18	**21c**/96
4	**9d**	CO_2Et	toluene	30	**20d**/71 **21d**/27
5	**9d**	CO_2Et	benzene	75	**20d**/68[c]

a) Based on the isolated products. b) The starting material **9b** was recovered in 28% yield.
c) The starting material **9d** was recovered in 22% yield.

The effects of the substituents at the amino nitrogen at the 2-position in pyridopyrimidines **23** on the azepine-ring formation were also examined. Heating 2-(*N*-allylanilino) substrate **23a** in refluxing xylene gave [1,3]oxazine **24** and a fully conjugated azepine **25** along with the unreacted **23a**. On the other hand, the reactions of 2-[*N*-allyl(ethoxycarbonyl)amino] **21b** and 2-[*N*-allyl(benzenesulfonyl)amino] substrate **21c** under similar conditions gave 2-allylamino-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**26**), the product owing to the fission of the N-CO and N-SO_2 bond in **23b** and **23c**, along with the unreacted starting materials (Scheme 7). According to the MO calculations of the reaction path utilizing PM3 method, the electron-withdrawing group on the amino nitrogen could be unfavorable to the 1,7-electrocyclic ring-closure process in the azepine-ring formation.[8]

Scheme 7.



23a: R^3= Ph
23b: R^3= CO_2Et
23c: R^3= SO_2Ph

24 **25** **26**

Conclusion

We have described here that both carbonyl and imine ene reactions take place at the periphery of pyrido[1,2-*a*]pyrimidone and pyridone systems leading to fused azepine derivatives efficiently and stereoselectively. At the same system and under the same reaction conditions, the imine ene reaction is superior to the carbonyl one. An electron-withdrawing group such as ethoxycarbonyl in the alkenyl moiety facilitates both imine and carbonyl ene reactions. However, the electron-withdrawing groups on the amino nitrogen make difficult to accomplish the azepine-ring formation. It should be also noteworthy that these features of the azepine-ring formations mentioned above are consistent with the results of MO calculations using PM3 method.[8]

Experimental Section

General Methods. Descriptions of instruments, general procedures, and chromatographic procedures have been published previously.[1]

Preparation of Starting Materials 9a-e, 15a-c, and 23a-c. 2-Alkenylamino-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehydes **9a-e** and **23a** were obtained by the reaction of 2-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde[9] with the corresponding amines similarly to the reported method for 6-alkenylamino-2,4-dioxo-1,2,3,4-tetrahydropyrimidine 5-carboxaldehydes.[1] In a similar manner, substrates **15a-c** were prepared from 4-chloro-1,6-dimethyl-2-oxo-1*H*-pyridine 3-carboxaldehyde, obtained through a Vilsmeier-Haack reaction of 3-hydroxy-1,6-dimethylpyridin-2(1*H*)-one,[10] and the amines. Substrates **23b,c** were obtained by the reaction of 2-allylamino-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**26**) with ethyl chloroformate and benzenesulfonyl chloride in the presence of sodium hydride, respectively. The structures of aldehydes **9**, **15**, and **23** were fully confirmed by their analytical and spectroscopic data. The selected data are summarized as follows:

2-(*N*-Allylbenzylamino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9a**): colorless needles from ethanol; mp 93-96 °C; ^{1}H NMR ($CDCl_3$) δ= 4.16 (2 H, d, *J*= 5.9 Hz, $NCH_2CH{=}CH_2$), 4.91 (2 H, s, CH_2Ph), 5.17 (1 H, d, *J*= 17.2 Hz, $NCH_2CH{=}CHH$), 5.20 (1 H, d, *J*= 10.2 Hz, $NCH_2CH{=}CHH$), 5.88 (1 H, tdd, *J*= 5.9, 10.2, 17.2 Hz, $NCH_2CH{=}CH_2$), 6.91 (1 H, dt, *J*= 1.3, 6.9 Hz, 7-H), 7.21-7.34 (6 H, ov, Ph and 9-H), 7.67 (1 H, ddd, *J*= 1.7, 6.9, 8.9 Hz, 8-H), 8.84 (1 H, dd, *J*= 1.7, 6.9 Hz, 6-H), 10.19 (1 H, s, CHO). Anal. Found: C, 71.34; H, 5.35; N, 13.14%. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.45; H, 5.37; N, 13.16%.

2-[*N*-Benzyl(*trans*-crotyl)amino]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9b**): colorless plates from hexane-benzene; mp 122-124 °C; ^{1}H NMR ($CDCl_3$) δ= 1.68 (3 H, d, *J*= 5.0 Hz, $NCH_2CH{=}CHMe$), 4.07 (2 H, d, *J*= 3.6 Hz, $NCH_2CH{=}CHMe$), 4.91 (2 H, s, CH_2Ph), 5.47-5.63 (2 H, ov, $NCH_2CH{=}CHMe$), 6.89 (1 H, dt, *J*= 1.3, 6.9 Hz, 7-H), 7.19-7.36 (6 H, ov, Ph and 9-H), 7.65 (1 H, ddd, *J*=

1.7, 6.9, 8.6 Hz, 8-H), 8.83 (1 H, ddd, *J*= 0.7, 1.7, 6.9 Hz, 6-H), 10.17 (1 H, s, CHO). Anal. Found: C, 72.12; H, 5.87; N, 12.49%. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.61%.

2-[*N*-Benzyl(*trans*-cinnamyl)amino]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9c**): yellow prisms from chloroform; mp 188-190 °C; ^{1}H NMR ($CDCl_3$) δ= 4.29 (2 H, d, *J*= 6.3 Hz, NCH_2CH=CHPh), 4.95 (2 H, s, CH_2Ph), 6.26 (1 H, td, *J*= 6.3, 15.8 Hz, NCH_2CH=CHPh), 6.45 (1 H, d, *J*= 15.8 Hz, NCH_2CH=CHPh), 6.91 (1 H, ddd, *J*= 1.3, 6.6, 7.3 Hz, 7-H), 7.20-7.36 (11 H, ov, Ph and 9-H), 7.68 (1 H, ddd, *J*= 1.7, 6.6, 8.9 Hz, 8-H), 8.85 (1H, ddd, *J*= 0.7, 1.7, 7.3 Hz, 6-H), 10.22 (1H, s, CHO). Anal. Found: C, 75.92; H, 5.37; N, 10.60%. Calcd for $C_{25}H_{21}N_3O_2$: C, 75.93; H, 5.35; N, 10.63%.

2-{*N*-Benzyl[*trans*-(3-ethoxycarbonyl)-2-propenyl]amino}-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9d**): colorless plates from hexane-benzene; mp 123-124 °C; ^{1}H NMR ($CDCl_3$) δ= 1.27 (3 H, t, *J*= 7.3 Hz, OCH_2CH_3), 4.17 (2 H, q, *J*= 7.3 Hz, OCH_2CH_3), 4.35 (2 H, dd, *J*= 1.6, 5.6 Hz, NCH_2CH=$CHCO_2$Et), 4.84 (2 H, s, CH_2Ph), 5.91 (1 H, td *J*= 1.6, 15.8 Hz, NCH_2CH=$CHCO_2$Et), 6.90 (1 H, td, *J*= 6.6, 15.8 Hz, NCH_2CH=$CHCO_2$Et), 6.96 (1 H, ddd, *J*= 1.3, 6.6, 7.3 Hz, 7-H), 7.20-7.36 (6H, ov, Ph and 9-H), 7.72 (1 H, ddd, *J*= 1.7, 6.6, 8.9 Hz, 8-H), 8.88 (1 H, ddd, *J*= 0.7, 1.7, 6.9 Hz, 6-H), 10.20 (1 H, s, CHO). Anal. Found: C, 67.56; H, 5.43; N, 10.66%. Calcd for $C_{22}H_{21}N_3O_4$: C, 67.50; H, 5.41; N, 10.74%.

2-[*N*-benzyl(3-methyl-2-propenyl)amino]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**9e**): colorless needles from hexane-benzene; mp 139-140 °C; ^{1}H NMR ($CDCl_3$) δ= 1.44, 1.62 (each 3 H, br s, $=CMe_2$), 4.11 (2 H, d, *J*= 6.6 Hz, NCH_2CH=CMe_2), 4.90 (2 H, s, CH_2Ph), 5.21 (1 H, m, NCH_2CH=CMe_2), 6.87 (1 H, dt, *J*= 1.3, 6.9 Hz, 7-H), 7.10-7.36 (6 H, ov, Ph and 9-H), 7.64 (1 H, ddd, *J*= 1.7, 6.7, 6.9 Hz, 8-H), 8.83 (1 H, dd, *J*= 1.0, 7.3 Hz, 6-H), 10.17 (1 H, s, CHO). Anal. Found: C, 72.46; H, 6.18; N, 12.11%. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 9.06; N, 12.10%.

4-(*N*-Allylbenzylamino)-1,6-dimethyl-2-oxo-1,2-dihydropyridine 3-carboxaldehyde (**15a**): yellow plates from hexane-benzene; mp 73-75 °C; ^{1}H NMR ($CDCl_3$) δ= 2.27 (3 H, s, 6-Me), 3.43 (3 H, s, 1-Me), 3.92 (2 H, d, *J*= 5.9 Hz, NCH_2CH=CH_2), 4.57 (2 H, s, CH_2Ph), 5.14 (1 H, d, *J*= 15.8 Hz, NCH_2CH=CHH), 5.20 (1 H, d, *J*= 8.9 Hz, NCH_2CH=CHH), 5.82 (1 H, s, 5-H), 5.84 (1 H, m, NCH_2CH=CH_2), 7.15-7.35 (5 H, ov, Ph), 10.14 (1 H, s, CHO). Anal. Found: C, 72.80; H, 6.96; N, 9.77%. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45%.

4-[*N*-Benzyl(*trans*-crotyl)amino]-1,6-dimethyl-2-oxo-1,2-dihydropyridine 3-carboxaldehyde (**15b**): yellow powder; mp 87-91 °C; ^{1}H NMR ($CDCl_3$) δ= 1.67 (3 H, d, *J*= 5.0 Hz, NCH_2CH=CHCH*Me*), 2.26 (3 H, s, 6-Me), 3.43 (3 H, s, 1-Me), 3.86 (2 H, d, *J*= 4.6 Hz, NCH_2CH=CHMe), 4.57 (2 H, s, CH_2Ph), 5.40-5.56 (2 H, ov, NCH_2CH=CHMe), 5.80 (1 H, s, 5-H), 7.15-7.34 (5 H, ov, Ph), 10.13 (1 H, s, CHO). Anal. Found: C, 73.48; H, 7.08; N, 9.22%. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; 9.03%.

4-[*N*-Benzyl(*trans*-cinnamyl)amino]-1,6-dimethyl-2-oxo-1,2-dihydropyridine 3-carboxaldehyde (**15c**): yellow oil; ^{1}H NMR ($CDCl_3$) δ= 2.27 (3 H, s, 6-Me), 3.44 (3 H, s, 1-Me), 4.08 (2 H, d, *J*= 6.3 Hz, NCH_2CH=CHPh), 4.62 (2 H, s, CH_2Ph), 5.84 (1 H, s, 5-H), 6.23 (1 H, td, *J*= 6.3, 15.8 Hz, NCH_2CH=CHPh), 6.43 (1 H, d, *J*= 15.8 Hz, NCH_2CH=CHPh), 7.17-7.37 (10 H, ov, Ph), 10.17 (1 H, s, CHO). Anal. Found: C, 77.84; H, 6.30; N, 7.31%. Calcd for $C_{24}H_{24}N_2O_2$: C, 77.39; H, 6.50; N, 7.52%.

2-(*N*-Allylanilino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**23a**): yellow plates from hexane-benzene; mp 122 °C; ^{1}H NMR ($CDCl_3$) δ= 4.77 (2 H, d, *J*= 5.3 Hz, NCH_2CH=CH_2), 5.13 (1 H, d, *J*= 10.2 Hz, NCH_2CH=CHH), 5.22 (1 H, d, *J*= 17.2 Hz, NCH_2CH=CHH), 6.00 (1 H, m, NCH_2CH=CH_2),

7.00 (1 H, ddd, *J*= 1.3, 6.6, 7.3 Hz, 7-H), 7.10-7.39 (6 H, ov, Ph and 9-H), 7.75 (1 H, ddd, *J*= 1.7, 6.6, 8.9 Hz, 8-H), 8.94 (1 H, dd, *J*= 1.7, 7.3 Hz, 6-H), 9.86 (1 H, s, CHO). Anal. Found: C, 70.88; H, 4.96; N, 13.71%. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.80; H, 4.95; N, 13.76%.

2-[*N*-Allyl(benzenesulfonyl)amino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**23b**): yellow prisms from hexane-benzene-ethanol; mp 192 °C (melted with decomposition); ^{1}H NMR ($CDCl_3$) δ= 4.30 (2 H, d, *J*= 6.6 Hz, $NCH_2CH=CH_2$), 5.04 (1 H, d, *J*= 10.2 Hz, $NCH_2CH=CHH$), 5.13 (1H, d, *J*= 16.8 Hz, $NCH_2CH=CHH$), 5.74 (1 H, tdd, *J*= 6.6, 10.2, 16.8 Hz, $NCH_2CH=CH_2$), 7.37 (1 H, dt, *J*= 1.3, 6.9 Hz, 7-H), 7.48-7.54 (3 H, ov, Ph), 7.62 (1 H, dd, *J*= 1.3, 8.6 Hz, 9-H), 7.82 (2 H, d, *J*= 7.3 Hz, Ph), 7.98 (1 H, ddd, *J*= 1.7, 6.9, 8.6 Hz, 8-H), 9.23 (1 H, dd, *J*= 1.7, 6.9 Hz, 6-H), 10.42 (1 H, s, CHO). Anal. Found: C, 58.69; H, 4.17; N, 11.13%. Calcd for $C_{18}H_{15}N_3O_4S$: C, 58.52; H, 4.09; N, 11.38%.

2-[*N*-Allyl(ethoxycarbonyl)amino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**23c**): pale yellow prisms from 2-propanol; mp 89-90 °C; ^{1}H NMR ($CDCl_3$) δ= 1.21 (3 H, t, *J*= 7.3 Hz, OCH_2CH_3), 4.19 (2 H, q, *J*= 7.3 Hz, OCH_2CH_3), 4.62 (2 H, d, *J*= 5.6 Hz, $NCH_2CH=CH_2$), 5.10 (1 H, dd, *J*= 1.3, 10.2 Hz, $NCH_2CH=CHH$), 5.23 (1 H, dd, *J*= 1.3, 17.2 Hz, $NCH_2CH=CHH$), 5.97 (1 H, m, $NCH_2CH=CH_2$), 7.28 (1 H, dd, *J*= 6.6, 6.9 Hz, 7-H), 7.61 (1 H, d, *J*= 8.9 Hz, 9-H), 7.95 (1 H, dd, *J*= 6.6, 8.9 Hz, 8-H), 9.12 (1 H, d, *J*= 6.9 Hz, 6-H), 10.29 (1 H, s, CHO). Anal. Found: C, 60.02; H, 5.11; N, 13.77%. Calcd for $C_{15}H_{15}N_3O_4$: C, 59.79; H, 5.02; N, 13.95%.

2-Allylamino-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine 3-carboxaldehyde (**26**): colorless needles from hexane-benzene; mp 119 °C; ^{1}H NMR ($CDCl_3$) δ= 4.26 (2 H, ddd, *J*= 1.3, 3.0, 6.9 Hz, $NCH_2CH=CH_2$), 5.19 (1 H, ddd, *J*= 1.3, 1.7, 10.2 Hz, $NCH_2CH=CHH$), 5.27 (1 H, ddd, *J*= 1.7, 3.0, 17.2 Hz, $NCH_2CH=CHH$), 5.97 (1 H, m, $NCH_2CH=CH_2$), 6.92 (1 H, dd, *J*= 6.6, 7.3 Hz, 7-H), 7.26 (1 H, d, *J*= 8.9 Hz, 9-H), 7.70 (1 H, dd, *J*= 6.6, 8.9 Hz, 8-H), 8.86 (1 H, d, *J*= 7.3 Hz, 6-H), 10.29 (1 H, s, CHO). Anal. Found: C, 63.04; H, 4.88; N, 18.60%. Calcd for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33%.

General Procedures for the Imine Ene Reactions. To a solution of aldehyde **9a** (0.10 g, 0.32 mmol) in benzene (5 ml) aniline (**10a**; 0.04 ml, 0.44 mmol) was added. The mixture was heated under reflux for 20 h and the solvent was evaporated to dryness. The residue was subjected to column chromatography on silica gel with hexane/ethyl acetate = 1:4 as eluent to give **11a** (0.1196 g, 97%). Product **11a** was recrystallized from hexane-benzene and obtained as pale yellow plates.

5-Anilino-1-benzyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**11a**): mp 169-170 °C; IR (KBr) 3440 (NH), 1645 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 2.71 (2 H, ov, 4-H), 4.38 (1 H, d, $J_{5\text{-NH}}$= 9.5 Hz, exchangable with D_2O, 5-NH), 4.77, 5.59 (each 1 H, each d, J_{gem}= 15.4 Hz, CH_2Ph), 4.86 (1 H, ddd, $J_{3\text{-}4}$= 3.7, $J_{3\text{-}4}$=5.1, $J_{2\text{-}3}$=11.0 Hz, 3-H), 5.77 (1 H, m, 5-H), 6.14 (1 H, d, $J_{2\text{-}3}$= 11.0 Hz, 2-H), 6.57-6.67 (3 H, ov, Ph), 6.92 (1 H, dd, $J_{8\text{-}9}$= 4.4, $J_{9\text{-}10}$= 6.6 Hz, 9-H), 7.07-7.36 (8 H, ov, Ph and 11-H), 7.52 (1 H, dd, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.8 Hz, 10-H), 8.93 (1 H, d, $J_{8\text{-}9}$= 4.4 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 33.3 (4-C), 45.8 (5-C), 55.4 (CH_2Ph), 103.7 (5a-C), 104.9 (3-C), 113.4, 116.7, 127.2, 127.6, 128.6, 129.1, 138.8, 146.8 (Ph-C), 113.5 (9-C), 125.0 (11-C), 127.6 (8-C), 130.9 (2-C), 135.5 (10-C), 147.8 (11a-C), 158.0 (12a-C), 158.3 (6-C); mass *m/z* 394 (M^+). Anal. Found: C, 76.18; H, 5.55; N, 14.13%. Calcd for $C_{25}H_{22}N_4O$: C, 76.12; H, 5.62; N, 14.20%.

1-Benzyl-5-isobutylamino-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**11b**): yellow prisms from hexane-benzene; mp 108-109 °C; IR (KBr) 3280 (NH), 1640 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 0.82 (3 H, d, $J_{CH\text{-}Me}$= 6.6 Hz, CH*Me*Me), 0.83 (3 H, d, $J_{CH\text{-}Me}$= 7.0 Hz, CHMe*Me*), 1.69 (1 H, m, C*H*Me$_2$), 1.88 (1 H, br, exchangable with D_2O, 5-NH), 2.23 (1 H, dd, J_{vic}= 7.0, J_{gem}= 11.0 Hz,

NHC*H*HCHMe$_2$), 2.43 (1 H, dd, J_{vic}= 6.6, J_{gem}= 11.0 Hz, NHCH*H*CHMe$_2$), 2.54 (1 H, td, $J_{3\text{-}4}$= $J_{4\text{-}5}$= 2.9, J_{gem}= 16.1 Hz, 4-H), 2.69 (1 H, ddd, $J_{4\text{-}5}$= 4.4, $J_{3\text{-}4}$= 4.8, J_{gem}= 16.1 Hz, 4-H), 4.89 (1 H, dddd, $J_{3\text{-}5}$= 1.1, $J_{3\text{-}4}$= 2.9, $J_{3\text{-}4}$= 4.8, $J_{2\text{-}3}$= 9.9 Hz, 3-H), 4.99 (1 H, ddd, $J_{3\text{-}5}$= 1.1, $J_{4\text{-}5}$= 2.9, $J_{4\text{-}5}$= 4.4 Hz, 5-H), 5.06, 5.32 (each 1 H, each d, J_{gem}= 15.4 Hz, C*H*$_2$Ph), 6.08 (1 H, d, $J_{2\text{-}3}$= 9.9 Hz, 2-H), 6.90 (1 H, ddd, $J_{9\text{-}11}$= 1.5, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 7.3 Hz, 9-H), 7.21-7.34 (6 H, ov, Ph and 11-H), 7.53 (1 H, ddd, $J_{8\text{-}11}$= 1.5, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.8 Hz, 10-H), 8.93 (1 H, dd, $J_{9\text{-}11}$= 1.5, $J_{8\text{-}9}$=7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 20.7, 21.0 (CH*Me*$_2$), 28.7 (*C*HMe$_2$), 32.7 (4-C), 51.6 (5-C), 54.9 (NH*C*H$_2$CHMe$_2$), 55.6 (*C*H$_2$Ph), 103.7 (5a-C), 106.6 (3-C), 113.2 (9-C), 124.9 (11-C), 127.2, 127.5, 128.5, 139.0 (Ph-C), 127.7 (8-C), 130.4 (2-C), 135.3 (10-C), 147.6 (11a-C), 157.4 (12a-C), 158.5 (6-C); mass *m/z* 374 (M^+). Anal. Found: C, 73.81; H, 7.02; N, 14.91%. Calcd for $C_{23}H_{26}N_4O$: C, 73.77; H, 7.00; N, 14.96%.

(4*RS*,5*RS*)-5-Anilino-1-benzyl-4-methyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**12a**); colorless prisms from propan-2-ol; mp 166-168 °C; IR (KBr) 3440 (NH), 1645 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 1.23 (3 H, d, $J_{4\text{-}Me}$= 6.9 Hz, 4-Me), 2.97 (1 H, m, 4-H), 4.14 (1 H, br, exchangable with D_2O, 5-NH), 4.57 (1 H, td, $J_{3\text{-}4}$= $J_{3\text{-}5}$= 2.0, $J_{2\text{-}3}$=10.2 Hz, 3-H), 4.75, 5.63 (each 1 H, each d, J_{gem}= 15.5 Hz, C*H*$_2$Ph), 5.55 (1 H, br, 5-H), 6.06 (1 H, dd, $J_{2\text{-}4}$= 2.6, $J_{2\text{-}3}$= 10.2 Hz, 2-H), 6.57 (1 H, t, $J_{m\text{-}p}$= 7.6 Hz, Ph-*p*), 6.65 (2 H, d, $J_{o\text{-}m}$= 8.6 Hz, Ph-*o*), 6.90 (1 H, ddd, $J_{9\text{-}11}$= 1.3, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 7.3 Hz, 9-H), 7.09 (2 H, dd, $J_{m\text{-}p}$= 7.6, $J_{o\text{-}m}$= 8.6 Hz, Ph-*m*), 7.21-7.34 (6 H, ov, Ph and 11-H), 7.50 (1 H, ddd, $J_{8\text{-}10}$= 1.7, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.92 (1 H, dd, $J_{8\text{-}10}$= 1.7, $J_{8\text{-}9}$= 7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 20.9 (4-Me), 37.4 (4-C), 50.8 (5-C), 55.3 (*C*H$_2$Ph), 104.1 (5a-C), 111.1 (3-C), 113.0, 116.3, 127.2, 127.5, 128.6, 129.1, 138.8, 147.5 (Ph-C), 113.4 (9-C), 124.9 (11-C), 127.5 (8-C), 129.2 (2-C), 135.4 (10-C), 147.7 (11a-C), 157.3 (12a-C), 158.2 (6-C). Anal. Found: C, 76.60; H, 5.94; N, 13.71%. Calcd for $C_{26}H_{24}N_4O$: C, 76.44; H, 5.92; N, 13.72%.

(4*RS*,5*RS*)-1-Benzyl-5-isobutylamino-4-methyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**12b**): yellow prisms from hexane-benzene; mp 104-106 °C; IR (KBr) 3300 (NH), 1645 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 0.80, 0.83 (each 3 H, each d, $J_{CH\text{-}Me}$= 6.6 Hz, CH*Me*$_2$), 1.28 (3 H, d, $J_{4\text{-}Me}$= 7.3 Hz, 4-Me), 1.41 (1 H, br, exchangable with D_2O, 5-NH), 1.61 (1 H, m, C*H*Me$_2$), 2.23 (1 H, dd, J_{vic}= 6.9, J_{gem}= 11.5 Hz, NHC*H*HCHMe$_2$), 2.34 (1 H, dd, J_{vic}= 6.6, J_{gem}= 11.5 Hz, NHCH*H*CHMe$_2$), 2.77 (1 H, m, 4-H), 4.58 (1 H, ddd, $J_{3\text{-}5}$= 1.7, $J_{3\text{-}4}$= 2.0, $J_{2\text{-}3}$= 10.2 Hz, 3-H), 4.72 (1 H, d, $J_{3\text{-}5}$= 1.7 Hz, 5-H), 5.01, 5.39 (each 1 H, each d, J_{gem}= 15.4 Hz, C*H*$_2$Ph), 5.97 (1 H, dd, $J_{2\text{-}4}$= 2.3, $J_{2\text{-}3}$= 10.2 Hz, 2-H), 6.89 (1 H, ddd, $J_{9\text{-}11}$= 1.0, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 7.3 Hz, 9-H), 7.21-7.35 (6 H, ov, Ph and 11-H), 7.52 (1 H, ddd, $J_{8\text{-}10}$= 1.7, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.6 Hz, 10-H), 8.88 (1 H, dd, $J_{8\text{-}10}$= 1.7, $J_{8\text{-}9}$= 7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 20.6, 20.8, 20.9 (CH*Me*$_2$ and 4-Me), 28.8 (*C*HMe$_2$), 37.7 (4-C), 55.2, 55.6 (NH*C*H$_2$CHMe$_2$ and *C*H$_2$Ph), 56.8 (5-C), 104.4 (5a-C), 113.1, 113.2 (3- and 9-C), 124.9 (11-C), 127.1, 127.5, 128.5, 139.1 (Ph-C), 127.7 (8-C), 128.2 (2-C), 135.1 (10-C), 147.4 (11a-C), 156.8 (12a-C), 158.5 (6-C). Anal. Found: C, 74.07; H, 7.09; N, 14.14%. Calcd for $C_{24}H_{28}N_4O$: C, 74.19; H, 7.26; N, 14.42%.

(4*RS*,5*RS*)-1-Benzyl-5-(*tert*-butylamino)-4-methyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**12c**): colorless prisms from hexane; mp 127-129 °C; IR (KBr) 3300 (NH), 1650 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 0.95 (9 H, s, C*Me*3), 1.18 (3 H, d, $J_{4\text{-}Me}$= 6.9 Hz, 4-Me), 1.41 (1 H, br, exchangable with D_2O, 5-NH), 2.68 (1 H, m, 4-H), 4.50 (1 H, d, $J_{2\text{-}3}$= 10.6 Hz, 3-H), 4.72-4.77 (2 H, ov, C*H*HPh and 5-H), 5.71 (1 H, d, J_{gem}= 15.2 Hz, CH*H*Ph), 5.98 (1 H, dd, $J_{2\text{-}4}$= 2.6, $J_{2\text{-}3}$= 10.6 Hz, 2-H), 6.90 (1 H, dd, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 7.3 Hz, 9-H), 7.21-7.43 (6 H, ov, Ph and 11-H), 7.55 (1 H, dd, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.88 (1 H, d, $J_{8\text{-}9}$= 7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 20.7 (4-Me), 30.2 (C*Me*3), 38.2 (4-C), 50.3 (5-C), 55.4 (NH*C*HMe3 and *C*H$_2$Ph), 109.2 (5a-C), 112.7 (3-C), 113.2 (9-C), 124.9 (11-C), 127.2, 127.8, 128.5, 139.1 (Ph-C), 127.6 (8-C), 128.3 (2-C), 134.9 (10-C), 147.2 (11a-C), 156.9 (12a-C), 157.7 (6-C). Anal. Found: C, 74.23; H, 7.41; N, 14.31%. Calcd for $C_{24}H_{28}N_4O$: C, 74.19; H, 7.26; N, 14.42%.

(4*RS*,5*SR*)-5-Anilino-1-benzyl-4-phenyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**13a**): yellow needles from ethanol; mp 222-223 °C; IR (KBr) 3380 (NH), 1640 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 4.12 (1 H, br, 4-H), 4.32 (1 H, br, exchangable with D_2O, 5-NH), 4.79, 5.72 (each 1 H, each d, J_{gem}= 15.2 Hz, C*H*$_2$Ph), 4.97 (1 H, td, $J_{3\text{-}4}$= $J_{3\text{-}5}$= 2.0, $J_{2\text{-}3}$= 10.6 Hz, 3-H), 5.81 (1 H, br, 5-H), 6.29 (1 H, dd, $J_{2\text{-}4}$= 2.6, $J_{2\text{-}3}$= 10.6 Hz, 2-H), 6.89-7.56 (18 H, ov, Ph and 5-, 9-, and 11-H), 8.94 (1 H, d, $J_{8\text{-}9}$= 6.9 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 47.6 (4-C), 51.6 (5-C), 55.4 (*C*H$_2$Ph), 103.9 (5a-C), 108.2 (3-C), 113.2, 116.4, 126.5, 127.4, 127.7, 128.1, 128.2, 128.7, 129.0, 138.7, 143.5, 147.0 (Ph-C), 113.6 (9-C), 125.1 (11-C), 127.6 (8-C), 130.6 (2-C), 135.6 (10-C), 147.9 (11a-C), 157.4 (12a-C), 158.1 (6-C). Anal. Found: C, 79.43; H, 5.68; N, 11.72%. Calcd for $C_{31}H_{26}N_4O$: C, 79.12; H, 5.57; N, 11.91%.

(4*RS*,5*SR*)-1-Benzyl-5-isobutylamino-4-phenyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**13b**): pale yellow oil; IR (NaCl) 3280 (NH), 1655 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 0.63, 0.70 (each 3 H, each d, $J_{CH\text{-}Me}$= 6.6 Hz, CH*Me*$_2$), 1.39-1.56 (2 H, ov, N*H*CH$_2$C*H*Me$_2$), 2.04-2.20 (2 H, ov, NHC*H*$_2$CHMe$_2$), 3.93 (1 H, br d, $J_{3\text{-}4}$= 2.6 Hz, 4-H), 4.92-4.99 (2 H, ov, 3- and 5-H), 5.04, 5.52 (each 1 H, each d, J_{gem}= 15.5 Hz, C*H*$_2$Ph), 6.17 (1 H, d, $J_{2\text{-}3}$= 10.2 Hz, 2-H), 6.90 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 7.3 Hz, 9-H), 7.19-7.57 (12 H, ov, Ph and 10- and 11-H), 8.90 (1 H, d, $J_{8\text{-}9}$= 6.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 20.4, 20.6 (CH*Me*$_2$), 28.5 (*C*HMe$_2$), 48.2 (4-C), 55.1, 55.6 (NHC*H*$_2$CHMe$_2$ and *C*H$_2$Ph), 57.3 (5-C), 103.9 (5a-C), 109.9 (3-C), 113.2 (9-C), 124.9 (11-C), 126.1, 127.1, 127.5, 127.8, 128.5, 128.6, 139.0, 144.5 (Ph-C), 127.7 (8-C), 129.7 (2-C) 135.3 (10-C), 147.5 (11a-C), 157.1 (12a-C), 158.4 (6-C); mass *m/z* 450 (M^+). Anal. Found: C, 77.30; H, 6.91; N, 11.94%. Calcd for $C_{29}H_{30}N_4O$: C, 77.30; H, 6.71; N, 12.44%.

(4*RS*,5*RS*)-5-Anilino-1-benzyl-4-ethoxycarbonyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**14a**): yellow needles from propan-2-ol; mp 163-166 °C; IR (KBr) 3345 (NH), 1725, 1645 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.02 (3 H, t, J_{vic}= 7.3 Hz, OCH$_2$C*H*$_3$), 3.64 (1 H, m, 4-H), 4.07-4.24 (3 H, ov, OC*H*$_2$CH$_3$ and NH), 4.76, 5.68 (each 1 H, each d, J_{gem}= 15.5 Hz, C*H*$_2$Ph), 5.22 (1 H, td, $J_{3\text{-}4}$= $J_{3\text{-}5}$= 2.0, $J_{2\text{-}3}$= 10.6 Hz, 3-H), 6.30 (1 H, dd, $J_{2\text{-}4}$= 2.6, $J_{2\text{-}3}$= 10.6 Hz, 2-H), 6.36 (1 H, br, 5-H), 6.56-6.66 (3 H, ov, Ph-*o,p*), 6.94 (1 H, dt, $J_{9\text{-}11}$= 1.3, $J_{8\text{-}9}$= $J_{9\text{-}10}$= 6.9 Hz, 9-H), 7.05-7.36 (8 H, ov, Ph-*m* and Ph and 11-H), 7.55 (1 H, dd, $J_{9\text{-}10}$= 6.9, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.94 (1 H, d, $J_{8\text{-}9}$= 6.9 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 14.2 (OCH$_2$*C*H$_3$), 47.2, 48.3 (4- and 5-C), 55.4 (*C*H$_2$Ph), 61.3 (O*C*H$_2$CH$_3$), 102.0(5a-C), 102.2 (3-C), 113.6, 117.1, 127.7, 128.7, 129.0, 138.5, 146.7 (Ph-C), 113.7 (9-C), 125.1 (11-C), 127.4 (8-C), 130.7 (2-C), 135.9 (10-C), 148.0 (11a-C), 157.2 (12a-C), 158.3 (6-C), 171.6 (CO). Anal. Found: C, 72.23; H, 5.56; N, 11.91%. Calcd for $C_{28}H_{26}N_4O_3$: C, 72.08; H, 5.62; N, 12.01%.

1-Benzyl-6,7-dimethyl-3-phenyl-1,2,3,4-tetrahydro-2,4-ethanopyrido[4,3-*d*]pyrimidin-5(6*H*)-one (**17a**): pale yellow crystals from hexane; mp 90-92 °C; IR (KBr) 1630 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.11 (3 H, s, 7-Me), 2.23 (2 H, ov, 10-H), 2.35 (2 H, ov, 9-H), 3.43 (3 H, s, 6-Me), 4.35, 4.47 (each 1 H, each d, J_{gem}= 16.9 Hz, C*H*$_2$Ph), 5.07 (1 H, d, $J_{4\text{-}10}$= 4.4 Hz, 4-H), 5.14 (1 H, d, $J_{2\text{-}9}$= 5.1 Hz, 2-H), 5.40 (1 H, s, 8-H), 6.76-7.28 (10 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.7 (7-Me), 30.2 (6-Me), 34.8, 34.9 (9- and 10-C), 52.1 (4-C), 53.7 (*C*H$_2$Ph), 74.4 (2-C), 95.4 (8-C), 103.9 (4a-C), 117.9, 119.5, 126.8, 127.3, 128.5, 128.8, 137.4, 144.4 (Ph-C), 145.6 (7-C), 149.2 (8a-C), 161.5 (5-C); mass *m/z* 371 (M^+). Anal. Found: C, 78.07; H, 7.13; N, 11.34%. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31%.

1-Benzyl-7,8-dimethyl-5-isobutylamino-4,5-dihydro-1*H*-pyrido[4,3-b]azepin-6(7*H*)-one (**16b**): yellow oil; IR (NaCl) 3280 (NH), 1625 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 0.86 (6 H, d, $J_{CH\text{-}Me}$= 6.6 Hz, CH*Me*$_2$), 1.73 (1 H, m, C*H*Me$_2$), 2.09 (1 H, br, exchangable with D_2O, 5-NH), 2.18 (3 H, s, 8-Me), 2.23 (1 H, dd, J_{vic}= 7.3, J_{gem}= 11.2 Hz, NHC*H*HCHMe$_2$), 2.46 (1 H, dd, J_{vic}= 6.3, J_{gem}= 11.2 Hz, NHCH*H*CHMe$_2$),

2.56-2.59 (1 H, ov, 4-H), 3.46 (3 H, s, 7-Me), 4.60-4.74 (3 H, ov, CH_2Ph and 3-H), 4.96 (1 H, br, 5-H), 5.71 (1 H, s, 9-H), 5.88 (1 H, d, $J_{2\text{-}3}$= 10.2 Hz, 2-H), 7.25-7.40 (5 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 20.8 (8-Me), 21.0, 21.2 (CH*Me*$_2$), 28.7 (*C*HMe$_2$), 31.2 (7-Me), 32.7 (4-C), 53.1 (NH*C*H$_2$CHMe$_2$), 55.2 (*C*H$_2$Ph), 57.5 (5-C), 100.1 (9-C), 104.4 (3-C), 115.7 (5a-C), 126.5, 127.4, 128.9, 137.6 (Ph-C), 131.3 (2-C), 142.8 (8-C), 151.7 (9a-C), 163.7 (6-C). The sample for elemental analysis could not be prepared because of its liability.

1-Benzyl-3-isobutyl-6,7-dimethyl-1,2,3,4-tetrahydro-2,4-ethanopyrido[4,3-*d*]pyrimidin-5(6*H*)-one (**17b**) : brown oil; IR (NaCl) 1630 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 0.84 (6 H, d, $J_{CH\text{-}Me}$= 6.6 Hz, CH*Me*$_2$), 1.59 (1 H, m, C*H*Me$_2$), 1.92-2.02 (2 H, ov, NHC*H*$_2$CHMe$_2$), 2.10-2.27 (4 H, ov, 9- and 10-H), 2.21 (3 H, s, 7-Me), 3.44 (3 H, s, 6-Me), 4.11 (1 H, d, $J_{4\text{-}10}$= 4.6 Hz, 4-H), 4.23 (1 H, d, $J_{2\text{-}9}$= 5.6 Hz, 2-H), 4.30, 4.43 (each 1 H, each d, J_{gem}= 16.8 Hz, C*H*$_2$Ph), 5.60 (1 H, s, 8-H), 7.25-7.38 (5 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 20.8, 20.9 (CH*Me*$_2$), 21.2 (7-Me), 26.9 (*C*HMe$_2$), 30.1 (6-Me), 35.0 (9- and 10-C), 51.8 (NC*H*$_2$CHMe$_2$), 54.5 (*C*H$_2$Ph), 56.5 (4-C), 77.0 (2-C), 94.8 (8-C), 102.0 (4a-C), 126.6, 127.2, 128.5, 138.4 (Ph-C), 144.0 (7-C), 149.1 (8a-C), 161.6 (5-C); mass *m/z* 351 (M$^+$). Anal. Found: C, 75.40; H, 8.64; N, 11.48%. Calcd for $C_{22}H_{29}N_3O$: C, 75.17; H, 8.32; N, 11.96%.

(2*RS*,4*RS*,10*RS*)-1-Benzyl-6,7,10-trimethyl-3-phenyl-1,2,3,4-tetrahydro-2,4-ethanopyrido[4,3-*d*]-pyrimidin-5(6*H*)-one (**17c**): colorless amorphous from hexane; mp 85-90 °C; IR (KBr) 1630 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 1.18 (3 H, d, $J_{10\text{-}Me}$= 6.9 Hz, 10-Me), 1.80 (1 H, ddd, $J_{9\text{-}10}$= 3.3, $J_{2\text{-}9}$= 5.3, J_{gem}= 12.9 Hz, 9-H*exo*), 2.10 (3 H, s, 7-Me), 2.45 (1 H, dd, $J_{9\text{-}10}$= 8.9, J_{gem}= 12.9 Hz, 9-H*endo*), 2.59 (1 H, m, 10-H), 3.42 (3 H, s, 6-Me), 4.34, 4.45 (each 1 H, each d, J_{gem}= 16.8 Hz, C*H*$_2$Ph), 4.74 (1 H, s, 4-H), 5.07 (1 H, d, $J_{2\text{-}9}$= 5.3 Hz, 2-H), 5.40 (1 H, s, 8-H), 6.76-7.28 (10 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.7 (7-Me), 22.9 (10-Me), 30.6 (6-Me), 43.1(9-C), 44.0 (10-C), 52.5 (*C*H$_2$Ph), 60.5 (4-C), 75.2 (2-C), 95.9 (8-C), 104.2 (4a-C), 118.2, 119.7, 127.4, 127.8, 129.0, 129.3, 138.0, 144.7 (Ph-C), 146.6 (7-C), 149.3 (8a-C), 162.0 (5-C); mass *m/z* 385 (M$^+$). Anal. Found: C, 77.84; H, 7.21; N, 10.95%. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90%.

General Procedures for the Carbonyl Ene Reactions. A solution of aldehyde **15a** (0.296 g, 1.00 mmol) in toluene (5 ml) was deoxgenated by flashing of argon stream for 30 min and heated under reflux for 24 h. The solvent was evaporated to dryness. The residue was subjected to column chromatography on silica gel with hexane/ethyl acetate= 1:3 as eluent to afford products **18a** (0.2316 g, 78%) and **19** (0.0196 g, 7%).

1-Benzyl-6,7-dimethyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[4,3-*d*][1,3]oxazin-5(6*H*)-one (**18a**): colorless needles from hexane-benzene; mp 168-170 °C; IR (KBr) 1635 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 2.05-2.27 (4 H, ov, 9- and 10-H), 2.19 (3 H, s, 7-Me), 3.42 (3 H, s, 6-Me), 4.44, 4.52 (each 1 H, each d, J_{gem}= 16.9 Hz, C*H*$_2$Ph), 5.12 (1 H, dd, $J_{4\text{-}10}$= 1.1, $J_{4\text{-}10}$= 3.7 Hz, 4-H), 5.39 (1 H, d, $J_{2\text{-}9}$= 2.2 Hz, 2-H), 5.58 (1 H, s, 8-H), 7.24-7.38 (5 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.1 (7-Me), 30.0 (6-Me), 35.1, 36.2 (9- and 10-C), 52.1 (*C*H$_2$Ph), 74.4 (4-C), 89.4 (2-C), 95.8 (8-C), 106.0 (4a-C), 126.4, 127.3, 128.7, 137.6 (Ph-C), 145.0 (7-C), 148.0 (8a-C), 160.2 (5-C); mass *m/z* 296 (M$^+$). Anal. Found: C, 72.86; H, 6.95; N, 9.62%. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45%.

1-Benzyl-7,8-dimethyl-1*H*-pyrido[4,3-*b*]azepin-6(7*H*)-one (**19**): orange needles from hexane-benzene; mp 154-156 °C; IR (KBr) 1620 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 2.24 (3 H, s, 8-Me), 3.43 (3 H, s, 7-Me), 4.32 (2 H, s, C*H*$_2$Ph), 5.15 (1 H, d, $J_{2\text{-}3}$= 7.6 Hz, 2-H), 5.19 (1 H, dd, $J_{3\text{-}4}$= 4.3, $J_{2\text{-}3}$= 7.6 Hz, 3-H), 5.59 (1 H, s, 9-H), 5.95 (1 H, dd, $J_{3\text{-}4}$= 4.3, $J_{4\text{-}5}$= 11.2 Hz, 4-H), 6.76 (1 H, d, $J_{4\text{-}5}$= 11.2 Hz, 5-H), 7.23-7.47 (5 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.1 (8-Me), 31.1 (7-Me), 54.9 (*C*H$_2$Ph), 100.2 (3-C), 115.9 (5a-C), 117.8

(9-C), 127.3, 127.7, 128.6, 146.6 (Ph-C), 129.3 (5-C), 131.4 (4-C), 137.0 (8-C), 139.0 (2-C), 161.0 (9a-C), 162.4 (6-C); mass *m/z* 278 (M^+). Anal. Found: C, 77.85; H, 6.52; N, 10.16%. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07%.

(2*RS*,4*SR*,10*SR*)-1-Benzyl-6,7,10-trimethyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[4,3-*d*][1,3]oxazin-5(6*H*)-one (**18b**): colorless needles from hexane-benzene; mp 168-169 °C; IR (KBr) 1635 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.11 (3 H, d, $J_{10\text{-Me}}$= 7.3 Hz, 10-Me), 2.05-1.68 (1 H, ddd, $J_{9\text{-}10}$= 2.9, $J_{2\text{-}9}$= 5.9, J_{gem}= 13.2 Hz, 9-H*exo*), 2.20 (3 H, s, 7-Me), 2.29 (1 H, dd, $J_{9\text{-}10}$= 8.8, J_{gem}= 13.2 Hz, 9-H*endo*), 2.61 (1 H, m, 10-H), 3.43 (3 H, s, 6-Me), 4.42, 4.51 (each 1 H, each d, J_{gem}= 16.9 Hz, CH_2Ph), 4.97 (1 H, s, 4-H), 5.14 (1 H, d, $J_{2\text{-}9}$= 5.9 Hz, 2-H), 5.58 (1 H, s, 8-H), 7.27-7.37 (5 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.3 (7- and 10-Me), 30.1 (6-Me), 43.8, 44.4 (9- and 10-C), 52.2 (*C*H_2Ph), 80.2 (4-C), 90.0 (2-C), 96.0 (8-C), 106.0 (4a-C), 126.6, 127.4, 128.8, 137.7 (Ph-C), 144.9 (7-C), 147.7 (8a-C), 160.2 (5-C); mass *m/z* 310 (M^+). Anal. Found: C, 73.81; H, 7.20; N, 9.00%. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03%.

(2*RS*,4*SR*,10*RS*)-1-Benzyl-6,7-dimethyl-10-phenyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[4,3-*d*][1,3]oxazin-5(6*H*)-one (**18c**): colorless plates from hexane-benzene; mp 199-200 °C; IR (KBr) 1630 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.21 (3 H, s, 7-Me), 2.32 (1 H, ddd, $J_{9\text{-}10}$= 2.9, $J_{2\text{-}9}$= 6.6, J_{gem}= 13.2 Hz, 9-H*exo*), 2.62 (1 H, dd, $J_{9\text{-}10}$= 8.8, J_{gem}= 13.2 Hz, 9-H*endo*), 3.44 (3 H, s, 6-Me), 3.71 (1 H, dd, $J_{9\text{-}10}$= 2.9, $J_{9\text{-}10}$= 8.8 Hz, 10-H), 4.48, 5.57 (each 1 H, each d, J_{gem}= 16.9 Hz, CH_2Ph), 5.28 (1 H, s, 4-H), 5.32 (1 H, d, $J_{2\text{-}9}$= 6.6 Hz, 2-H), 5.62 (1 H, s, 8-H), 7.17-7.39 (10 H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ= 21.3 (7-Me), 30.1 (6-Me), 44.2 (9-C), 52.3 (*C*H_2Ph), 55.4 (10-C), 80.8 (4-C), 90.0 (2-C), 95.8 (8-C), 105.9 (4a-C), 126.2, 126.6, 126.9, 127.4, 128.3, 128.8, 137.6, 145.3 (Ph-C), 145.0 (7-C), 147.6 (8a-C), 160.2 (5-C); mass *m/z* 372 (M^+). Anal. Found: C, 77.65; H, 6.56; N, 7.57%. Calcd for $C_{24}H_{24}N_2O_2$: C, 77.39; H, 6.60; N, 7.52%.

A solution of aldehyde **9a** (0.100 g, 0.31 mmol) in xylene (5 ml) was similarly deoxygenated and heated under reflux for 20 h. The solvent was evaporated to dryness. The residue was subjected to column chromatography on silica gel with hexane/ethyl acetate = 3:2, 1:1, and 2:3 as eluent to afford products **22** (0.0401 g, 42%), **21a** (0.0330 g, 33%), and **20a** (0.0224 g, 22%) , respectively.

1-Benzyl-5-hydroxy-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**20a**): colorless needles from hexane-benzene; mp 146-147 °C; IR (KBr) 3380 (OH), 1610 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.55-2.72 (2 H, ov, 4-H), 4.00 (1 H, br, exchanged with D_2O, 5-OH), 5.14, 5.21 (each 1 H, each d, J_{gem}= 14.8 Hz, CH_2Ph), 5.21 (1 H, ddd, $J_{3\text{-}4}$= 5.6, $J_{3\text{-}4}$= 6.9, $J_{2\text{-}3}$= 8.9 Hz, 3-H), 5.58 (1 H, br, 5-H), 6.12 (1 H, d, $J_{2\text{-}3}$= 8.9 Hz, 2-H), 6.89 (1 H, ddd, $J_{9\text{-}11}$= 1.3, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 7.3 Hz, 9-H), 7.21-7.36 (6 H, ov, Ph and 11-H), 7.55 (1 H, ddd, $J_{8\text{-}10}$= 1.7, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.83 (1 H, ddd, $J_{8\text{-}11}$= 1.0, $J_{8\text{-}10}$= 1.7, $J_{8\text{-}9}$= 7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 33.0 (4-C), 54.6 (*C*H_2Ph), 67.2 (5-C), 102.3 (5a-C), 110.3 (3-C), 113.3 (9-C), 124.8 (11-C), 127.1, 127.4, 128.5, 138.6 (Ph-C), 127.1 (8-C), 132.6 (2-C), 135.8 (10-C), 147.3 (11a-C), 156.6 (12a-C), 159.1 (6-C); mass *m/z* 319 (M^+), 301 (M^+ - H_2O). Anal. Found: C, 71.57; H, 5.33; N, 13.07%. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.45; H, 5.37; N, 13.16%.

1-Benzyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[1',2':1,2]pyrimido[4,5-*d*][1,3]oxazin-5(5*H*)-one (**21a**): yellow prisms from hexane-benzene; mp 158-159 °C; IR (KBr) 1665 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.07-2.28 (4 H, ov, 12- and 13-H), 4.76, 5.07 (each 1 H, each d, J_{gem}= 15.8 Hz, CH_2Ph), 5.28 (1 H, d, $J_{4\text{-}13}$= 4.4 Hz, 4-H), 5.57 (1 H, dd, $J_{2\text{-}12}$= 2.9, $J_{2\text{-}12}$= 3.7 Hz, 2-H), 6.90 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{7\text{-}8}$= 8.1 Hz, 8-H), 7.26-7.35 (6 H, ov, Ph and 10-H), 7.56 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 8.8 Hz, 9-H), 8.93 (1 H, d, $J_{7\text{-}8}$= 8.1 Hz, 7-H); ^{13}C NMR ($CDCl_3$) δ= 35.6, 35.7 (12- and 13-C), 48.6 (*C*H_2Ph), 74.6 (4-C), 88.0 (2-C), 95.8 (4a-C), 112.8 (8-C), 124.4 (10-C), 127.4, 127.8, 128.7, 138.0 (Ph-C), 127.9 (7-C), 135.9 (9-C), 150.6 (10a-C),

153.7 (11a-C), 155.1 (5-C); mass *m/z* 319 (M^+). Anal. Found: C, 71.60; H, 5.41; N, 13.20%. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.45; H, 5.37; N, 13.16%.

1-Benzyl-pyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**22**): red needles from hexane-benzene; mp 148-150 °C; IR (KBr) 1655 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 4.68 (2 H, s, C*H*$_2$Ph), 5.07 (1 H, dd, $J_{3\text{-}4}$= 5.1, $J_{2\text{-}3}$= 8.1 Hz, 3-H), 5.13 (1 H, d, $J_{2\text{-}3}$= 8.1 Hz, 2-H), 5.69 (1 H, dd, $J_{3\text{-}4}$= 5.1, $J_{4\text{-}5}$= 11.0 Hz, 4-H), 6.37 (1 H, d, $J_{4\text{-}5}$= 11.0 Hz, 5-H), 6.95 (1 H, dd, $J_{8\text{-}9}$= 5.1, $J_{9\text{-}10}$= 6.6 Hz, 9-H), 7.22-7.59 (7 H, ov, Ph and 10- and 11-H), 8.87 (1 H, d, $J_{8\text{-}9}$= 5.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 53.9 (*C*H$_2$Ph), 103.9 (5a-C), 115.1 (9-C), 117.6 (3-C), 125.4 (11-C), 127.5 (8-C), 128.3, 128.4, 128.9, 138.5 (Ph-C), 129.0 (5-C), 129.3 (4-C), 136.9 (10-C), 138.4 (2-C), 150.0 (11a-C), 157.2 (12a-C), 167.8 (6-C); mass *m/z* 301 (M^+), 210 (M^+ - C_7H_7). Anal. Found: C, 75.59; H, 4.83; N, 13.79%. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.95%.

(4*RS*,5*RS*)1-Benzyl-5-hydroxy-4-methyl-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**20b**): colorless needles from hexane-benzene; mp 164-165 °C; IR (KBr) 3380 (OH), 1615 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.28 (3 H, d, $J_{4\text{-Me}}$= 7.3 Hz, 4-Me), 2.74-2.80 (2 H, ov, OH and 4-H), 4.82 (1 H, dd, $J_{3\text{-}4}$= 2.9, $J_{2\text{-}3}$= 9.5 Hz, 3-H), 5.05, 5.32 (each 1 H, each d, J_{gem}= 15.4 Hz, C*H*$_2$Ph), 5.51 (1 H, br d, $J_{5\text{-OH}}$= 7.3 Hz, 5-H), 6.05 (1 H, dd, $J_{2\text{-}4}$= 2.2, $J_{2\text{-}3}$= 9.5 Hz, 2-H), 6.90 (1 H, dd, $J_{9\text{-}10}$= 6.6, $J_{8\text{-}9}$= 8.1 Hz, 9-H), 7.26-7.36 (6 H, ov, Ph and 11-H), 7.54 (1 H, dd, $J_{9\text{-}10}$= 6.6, $J_{10\text{-}11}$= 8.8 Hz, 10-H), 8.85 (1 H, d, $J_{8\text{-}9}$= 8.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 19.4 (4-Me), 38.5 (4-C), 55.4 (*C*H$_2$Ph), 71.7 (5-C), 102.4 (5a-C), 113.7 (9-C), 114.9 (3-C), 125.3 (11-C), 127.6, 127.8, 128.9, 139.1 (Ph-C), 127.8 (8-C), 130.3 (2-C), 136.2 (10-C), 148.1 (11a-C), 157.1 (12a-C), 159.2 (6-C); mass *m/z* 333 (M^+), 315 (M^+ - H_2O). Anal. Found: C, 72.04; H, 5.78; N, 12.78%. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.61%.

(2*RS*,4*SR*,13*SR*)-1-Benzyl-13-methyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[1',2':1,2]pyrimido[4,5-*d*]-[1,3]oxazin-5(5*H*)-one (**21b**): yellow prisms from hexane-benzene; mp 163-165 °C; IR (KBr) 1660 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.13 (3 H, d, $J_{13\text{-Me}}$= 6.6 Hz, 13-Me), 1.67 (1 H, ddd, $J_{12\text{-}13}$= 2.9, $J_{2\text{-}12}$= 5.9, J_{gem}= 13.2 Hz, 12-H*exo*), 2.29 (1 H, dd, $J_{12\text{-}13}$= 8.8, J_{gem}= 13.2 Hz, 12-H*endo*), 2.62 (1 H, m, 13-H), 4.74, 5.05 (each 1 H, each d, J_{gem}= 15.4 Hz, C*H*$_2$Ph), 5.13 (1 H, s, 4-H), 5.29 (1 H, d, $J_{2\text{-}12}$= 5.9 Hz, 2-H), 6.90 (1 H, ddd, $J_{8\text{-}10}$= 1.5, $J_{8\text{-}9}$= 6.6, $J_{7\text{-}8}$= 7.3 Hz, 8-H), 7.26-7.36 (6 H, ov, Ph and 10-H), 7.55 (1 H, ddd, $J_{7\text{-}9}$= 1.5, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 8.8 Hz, 9-H), 8.92 (1 H, ddd, $J_{7\text{-}9}$= 0.7, $J_{7\text{-}9}$= 1.5, $J_{7\text{-}8}$= 7.3 Hz, 7-H); ^{13}C NMR ($CDCl_3$) δ= 21.5 (13-Me), 43.7 (12-C), 44.1 (13-C), 48.4 (*C*H$_2$Ph), 80.1 (4-C), 88.3 (2-C), 95.2 (4a-C), 112.7 (8-C), 124.3 (10-C), 127.3, 127.6, 128.6, 137.8 (Ph-C), 127.6 (7-C), 135.8 (9-C), 150.4 (10a-C), 153.6 (11a-C), 154.5 (5-C); mass *m/z* 333 (M^+). Anal. Found: C, 72.34; H, 5.86; N, 12.69%. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.61%.

(2*RS*,4*SR*,13*RS*)-1-Benzyl-13-phenyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[1',2':1,2]pyrimido[4,5-*d*]-[1,3]oxazin-5(5*H*)-one (**21c**): pale brown prisms from hexane-benzene; mp 193-195 °C; IR (KBr) 1665 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.26 (1 H, ddd, $J_{12\text{-}13}$= 3.7, $J_{2\text{-}12}$= 5.9, J_{gem}= 13.2 Hz, 12-H*exo*), 2.65 (1 H, dd, $J_{12\text{-}13}$= 8.8, J_{gem}= 13.2 Hz, 12-H*endo*), 3.71 (1 H, dd, $J_{12\text{-}13}$= 3.7, $J_{12\text{-}13}$= 8.8 Hz, 13-H), 4.79, 5.14 (each 1 H, each d, J_{gem}= 15.8 Hz, C*H*$_2$Ph), 5.46 (1 H, d, $J_{2\text{-}12}$= 5.9 Hz, 2-H), 5.48 (1 H, s, 4-H), 6.90 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{7\text{-}8}$= 8.1 Hz, 8-H), 7.19-7.39 (11 H, ov, Ph and 10-H), 7.56 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 8.8 Hz, 9-H), 8.93 (1 H, d, $J_{7\text{-}8}$= 8.1 Hz, 7-H); ^{13}C NMR ($CDCl_3$) δ= 45.3 (12-C), 48.6 (*C*H$_2$Ph), 54.8 (13-C), 80.9 (4-C), 88.4 (2-C), 95.3 (4a-C), 112.7 (8-C), 124.4 (10-C), 126.4, 126.8, 127.4, 127.7, 128.5, 128.6, 137.8, 145.0 (Ph-C), 127.8 (7-C), 136.0 (9-C), 150.6 (10a-C), 153.6 (11a-C), 154.6 (5-C); mass *m/z* 395 (M^+). Anal. Found: C, 76.21; H, 5.44; N, 10.38%. Calcd for $C_{25}H_{21}N_3O_2$: C, 75.93; H, 5.35; N, 10.63%.

(4*RS*,5*RS*)-1-Benzyl-4-ethoxycarbonyl-5-hydroxy-4,5-dihydropyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**20d**): pale yellow prisms from hexane-benzene; mp 117-119 °C; IR (KBr) 3340 (OH), 1730, 1615 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.32 (3 H, t, J_{vic}= 7.3 Hz, OCH_2CH_3), 3.23 (1 H, br, exchangable with D_2O, 5-OH), 3.56 (1 H, m, 4-H), 4.25 (2 H, q, J_{vic}= 7.3 Hz, OCH_2CH_3), 5.10 (1 H, d, J_{gem}= 15.5 Hz, CHHPh), 5.31-5.37 (2 H, ov, CHHPh and 3-H), 6.15 (1 H, br, 5-H), 6.24 (1 H, dd, $J_{2\text{-}4}$= 2.3, $J_{2\text{-}3}$= 9.9 Hz, 2-H), 6.93 (1 H, t, $J_{8\text{-}9}$= $J_{9\text{-}10}$= 6.9 Hz, 9-H), 7.26-7.36 (6 H, ov, Ph and 11-H), 7.60 (1 H, dd, $J_{9\text{-}10}$= 6.9, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.88 (1 H, d, $J_{8\text{-}9}$= 6.9 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 14.2 (OCH_2CH_3), 48.8 (4-C), 55.2 (CH_2Ph), 61.3 (OCH_2CH_3), 67.9 (5-C), 100.4 (5a-C), 105.8 (3-C), 113.5 (9-C), 124.9 (11-C), 127.2 (12-C), 127.4, 127.5, 128.6, 138.4 (Ph-C), 131.4 (2-C), 136.2 (10-C), 147.9 (11a-C), 156.6 (12a-C), 158.7 (6-C). Anal. Found: C, 64.58; H, 5.51; N, 10.58%. Calcd for $C_{22}H_{21}N_3O_4$: C, 67.50; H, 5.41; N, 10.74%.

(2*RS*,4*SR*,13*SR*)-1-Benzyl-13-ethoxycarbonyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[1',2':1,2]pyrimido-[4,5-*d*][1,3]oxazin-5(5*H*)-one (**21d**): colorless needles from hexane-benzene; mp 182-183 °C; IR (KBr) 1715, 1665 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 1.30 (3 H, t, J_{vic}= 7.3 Hz, OCH_2CH_3), 2.26 (1 H, dd, $J_{12\text{-}13}$= 9.2, J_{gem}= 13.5 Hz, 12-H*endo*), 2.62 (1 H, ddd, $J_{12\text{-}13}$= 3.3, $J_{2\text{-}12}$= 5.9, J_{gem}= 13.5 Hz, 12-H*exo*), 3.37 (1 H, dd, $J_{12\text{-}13}$= 3.3, $J_{12\text{-}13}$= 9.2 Hz, 13-H), 4.20 (2 H, q, J_{vic}= 7.3 Hz, OCH_2CH_3), 4.83, 5.01 (each 1 H, each d, J_{gem}= 15.5 Hz, CH_2Ph), 5.37 (1 H, d, $J_{2\text{-}12}$= 5.9 Hz, 2-H), 5.82 (1 H, s, 4-H), 6.93 (1 H, ddd, $J_{8\text{-}10}$= 1.3, $J_{8\text{-}9}$= 6.6, $J_{7\text{-}8}$= 7.3 Hz, 8-H), 7.24-7.35 (6 H, ov, Ph and 10-H), 7.59 (1 H, dd, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 8.6 Hz, 9-H), 8.93 (1 H, d, $J_{7\text{-}8}$= 7.3 Hz, 7-H); ^{13}C NMR ($CDCl_3$) δ= 14.6 (OCH_2CH_3), 38.8 (12-C), 49.1 (13-C), 53.7 (CH_2Ph), 61.7 (OCH_2CH_3), 77.4 (4-C), 88.4 (2-C), 94.2 (4a-C), 113.4 (8-C), 124.9 (10-C), 127.9 (7-C), 127.4, 129.2, 138.0 (Ph-C), 136.7 (9-C), 151.2 (10a-C), 154.0 (11a-C), 155.1 (5-C), 172.7 (CO). Anal. Found: C, 67.60; H, 5.39; N, 10.64%. Calcd for $C_{22}H_{21}N_3O_4$: C, 67.50; H, 5.41; N, 10.74%.

The thermal reaction of aldehyde **23a** in deoxygenated xylene solution for 50 h gave products **24** (32%) and **25** (31%) along with the unreacted **23a** (33%).

1-Phenyl-1,4-dihydro-2,4-ethano-2*H*-pyrido[1',2':1,2]pyrimido-4,5-*d*][1,3]oxazin-5(5*H*)-one (**24**): pale yellow prisms from hexane-benzene; mp 165-166 °C; IR (KBr) 1670 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.24-2.50 (4 H, ov, 12- and 13-H), 5.65 (1 H, d, $J_{4\text{-}13}$= 5.6 Hz, 4-H), 5.68 (1 H, d, $J_{2\text{-}12}$= 5.3 Hz, 2-H), 6.91 (1 H, ddd, $J_{8\text{-}10}$= 1.3, $J_{8\text{-}9}$= 6.6, $J_{7\text{-}8}$= 7.3 Hz, 8-H), 7.19-7.45 (6 H, ov, Ph and 10-H), 7.52 (1 H, ddd, $J_{7\text{-}9}$= 1.7, $J_{8\text{-}9}$= 6.6, $J_{9\text{-}10}$= 8.9 Hz, 9-H), 8.93 (1 H, dd, $J_{7\text{-}9}$= 1.7, $J_{7\text{-}8}$= 7.3 Hz, 7-H); ^{13}C NMR ($CDCl_3$) δ= 35.4, 36.2 (12- and 13-C), 74.6 (4-C), 91.5 (2-C), 97.0 (4a-C), 113.2 (8-C), 124.8 (10-C), 126.1, 126.4, 129.1, 141.3 (Ph-C), 127.5 (7-C), 135.7 (9-C), 150.1 (10a-C), 154.3 (11a-C), 154.3 (5-C). Anal. Found: C, 70.87; H, 5.01; N, 13.71%. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.80; H, 4.95; N, 13.76%.

1-Phenylpyrido[1',2':1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (**25**): red prisms from hexane-benzene; mp 158 °C; IR (KBr) 1665 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ= 5.75 (1 H, dd, $J_{3\text{-}4}$= 5.3, $J_{2\text{-}3}$= 7.3 Hz, 3-H), 6.09 (1 H, d, $J_{2\text{-}3}$= 7.3 Hz, 2-H), 6.18 (1 H, dd, $J_{3\text{-}4}$= 5.3, $J_{4\text{-}5}$= 11.2 Hz, 4-H), 6.90 (1 H, d, $J_{4\text{-}5}$= 11.2 Hz, 5-H), 7.00-7.38 (7 H, ov, Ph and 9- and 11-H), 7.57 (1 H, ddd, $J_{8\text{-}10}$= 1.7, $J_{9\text{-}10}$= 6.7, $J_{10\text{-}11}$= 8.9 Hz, 10-H), 8.98 (1 H, ddd, $J_{8\text{-}11}$= 0.7, $J_{8\text{-}10}$= 1.7, $J_{8\text{-}9}$= 7.3 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ= 108.4 (5a-C), 115.2 (9-C), 117.7, 122.2, 128.8, 144.0 (Ph-C), 120.7 (3-C), 125.7 (11-C), 127.7 (8-C), 127.8 (5-C), 128.6 (4-C), 133.1 (2-C), 136.0 (10-C), 150.1 (11a-C), 158.0 (12a-C), 160.3 (6-C). Anal. Found: C, 75.34; H, 4.55; N, 14.60%. Calcd for $C_{18}H_{13}N_3O$: C, 75.24; H, 4.56; N, 14.63%.

X-Ray Single-crystal Structure Analyses of Dihydroazepine 12a and [1,3]Oxazine 18c. Single crystals of compound **12a** and **18c** were obtained from propan-2-ol as prisms. A crystal of approximate

dimensions 0.160 x 0.200 x 0.680 mm was used for data collection of **12c**, one of 0.380 x 0.600 x 1.000 of **18c**. All measurements were made on a Rigaku AFC5S diffractometer by employing graphite-monochromated Mo-Kα radiation. The unit-cell dimensions were obtained by least-squares analysis of 15 reflections within the range of $8.82 < 2\theta < 14.25°$ for compound **12c**, and 24 reflections within the range of $35.87 < 2\theta < 39.54°$ for compound **18c**, respectively. The crystal data for compound **12c** are given: crystal system: triclinic; space group: $P\bar{1}$ (#2); cell constants: *a*: 10.610 (8)Å, *b*: 11.49 (1)Å, *c*: 9.788 (8)Å, V: 1079 (2)Å^3; α: 11.216 (6)°, β: 96.36 (7)°, γ: 77.56 (6)°; Z value: 2; Dc: 1.257 g cm^{-3}. The crystal data for compound **18c** are shown as follows: crystal system: triclinic; space group: $P\bar{1}$ (#2); cell constants: *a*: 10.765 (3)Å, *b*: 12.010 (2)Å, *c*: 8.065 (5)Å; V: 977.5 (5)Å^3, α: 106.94 (2)°, β: 97.23 (3)°, γ: 79.41 (2)°; Z value: 2; Dc: 1.265 g cm^{-3}. The ω-2θ scan technique to a maximum 2θ-value of 55° was used. Scans of $(1.68 + 0.33 \tan \theta)°$ were made at a speed 32° min^{-1} for compound **12c** and of $(1.63 + 0.30 \tan \theta)°$ at a speed of 32° min^{-1} for compound **18c**. A total of 5229 observed reflections (unique: 4958; R_{int}= 0.065) for **12c** and 4729 observed reflections (unique: 4488; R_{int}= 0.018) for **18c** was collected. All calculations were performed using TEXAN program.[11] Atoms other than hydrogen were refined anisotropically. The structures were solved by direct methods (MITHRIL)[12] and refined by least-squares to *R* 0.056 (compound **12c**) and 0.044 (compound **18c**). ORTEP[13] drawings of compounds **12c** and **18c** are shown in Figs. 1 and 2.[7]

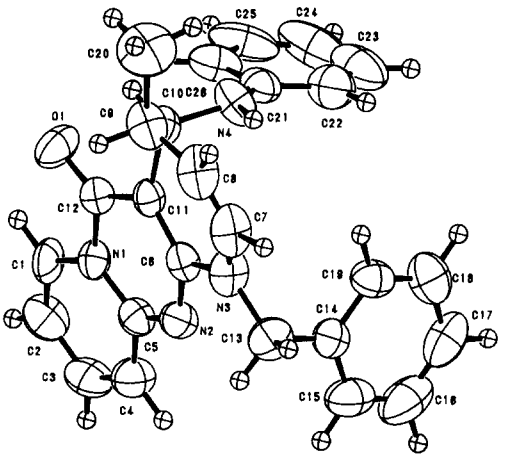


Fig. 1. ORTEP drawing of compound **12c** with crystallographic numbering scheme.

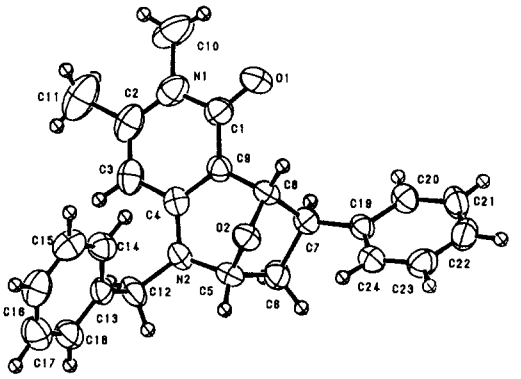


Fig. 2. ORTEP drawing of compound **18c** with crystallographic numbering scheme.

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