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Competitive thermal ene reaction and Diels–Alder reactions of 2-[*N*-(alk-2-enyl)benzylamino]-3-vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones

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Abstract—Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-(2-substituted and 2,2-disubstituted)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones gave azepine, the desired ene products, and/or pyran derivatives. The formation of the latter was responsible for the [4+2] cycloaddition reaction between the α,β-unsaturated ester carbonyl moiety as a diene part and the alkenylamino moiety as an ene one. The reaction features depended upon the kinds of substituents both on the vinyl and alkenyl counterparts; strongly electron-withdrawing substituents on the vinyl moiety or an electron-donating substituent on the alkenyl one changed the reaction feature from the ene reaction to the hetero Diels–Alder reaction.

1. Introduction

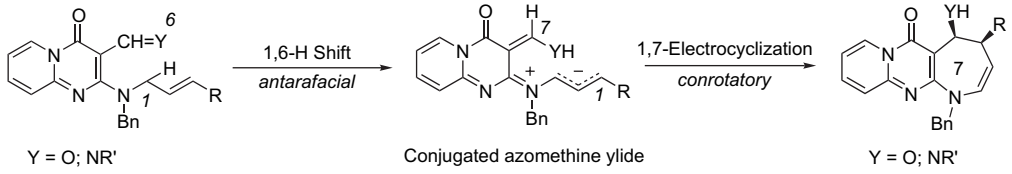
Recently, we have reported on a facile and stereoselective azepine-ring formation at the periphery of heterocyclic systems via thermal imine- and carbonyl-ene reactions[1] classified as a 7-(1,4) intramolecular ene reaction (Scheme 1).[2]

In order to develop the ene reaction, our next concern was focused on the reaction of the similar substrates bearing vinyl moiety as an enophile. The thermal reaction of 2-(*N*-alk-2-enyl)-benzylamino-3-(2-substituted and 2,2-disubstituted)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones gave the desired ene products and the hetero Diels–Alder adducts. The latter products, therein, were formed by the [4+2] cycloaddition reaction of the α,β-unsaturated ester carbonyl moiety of the substituted vinyl as a diene and the alkenyl moiety as a dienophile. The reaction features depended on the kinds of the substituents both on the vinyl and alkenylamino parts; when electron-withdrawing substituents such as cyano or ethoxycarbonyl group resided on the vinyl moiety or an electron-donating substituent such as methyl or phenyl one did on the alkenyl moiety, the hetero Diels–Alder reaction was competing with or superior to the ene reaction. The scope and limitations of these thermal reactions will be discussed.

2. Results and discussion

2.1. Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones

The starting 3-vinylpyridopyrimidines **2**, **3**, and **4** were prepared by the reaction of 2-(*N*-allylbenzylamino)-3-formylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones **1** with a Horner–



Scheme 1. *Reaction*: (i) 7-(1,4) intramolecular ene reaction.

Keywords: Competitive reaction; Ene reaction; Diels–Alder reaction.
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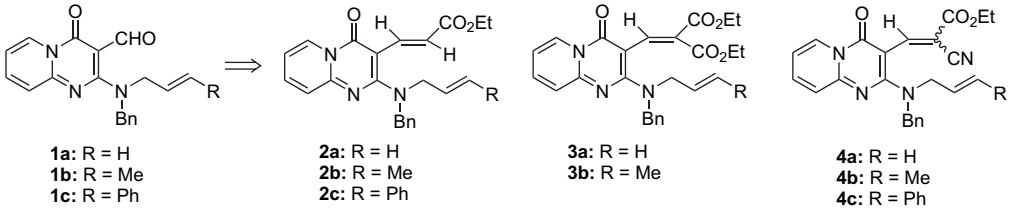
Emmons reagent for **2**, with diethyl malonate in refluxing benzene in the presence of piperidine and acetic acid[3] for **3**, and with ethyl cyanoacetate in ethanol in the presence of potassium carbonate for **4** (Scheme 2). Vinyl substrates **2a** and **4a** were composed of inseparable mixtures of *E*- and *Z*-isomers and the *E*/*Z* ratios were deduced to be >19:1 for **2** and >6:1 for **4** from their ^{1}H NMR spectral data.

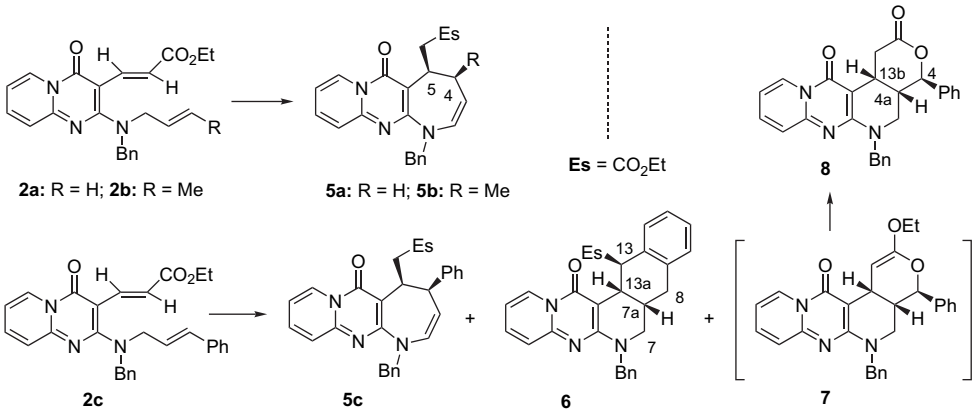
The reaction of vinyl substrates **2a** in refluxing xylene gave the desired ene product, pyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepine **5a** in good yields. The structure of **5a** was established by spectroscopic data in comparison with those of the related azepine derivatives.[1] In order to obtain further information on the reaction features, substrates **2b** and **2c** were allowed to react. While the thermal reaction of **2b** in refluxing xylene gave only azepine **5b**, the similar reaction of **2c** yielded a mixture of three isomeric products, azepine **5c**, homo Diels–Alder adduct **6**, and hetero Diels–Alder adduct **7**, in a good total yield (Scheme 3). The structure of **6** was also accomplished on the basis of its spectroscopic data; the ^{1}H–^{1}H COSY spectra of **6** elucidated two sets of alignment of methylene (δ=ca. 3.0; 7-H$_2$)-methine (2.49; 7a-H)-methylene protons (2.64 and 3.30; 8-H$_2$) and methine (2.49; 7a-H)-methine (4.01; 13a-H)-methine one (3.89; 13-H). This suggested that the framework of **6** was deduced to be benzo[*g*]pyrido[1′,2′:1,2]pyrimido[4,5-*c*]isoquinoline arising from the Diels–Alder reaction between the styrene and vinyl moiety of **2c**. The configurations among the 7a-H, 13a-H, and 13-H were deduced to be cis (J_{7a-13a}= 4.6 Hz) and trans (J_{13a-13}=8.6 Hz) compared with the coupling constants of the related ring systems obtained by the intramolecular Diels–Alder reaction of the substrates bearing styrene moiety as diene components such as *N*-(*E*)-cinnamylmethyl fumaramic acid ethyl ester.[4] On the other hand, product **7** was not so stable and converted to **8** during the chromatographic purification on silica gel. The structure of **8** was also established by its spectroscopic data; the ^{1}H–^{1}H COSY spectra of **8** elucidated two sets of alignment of methylene (δ=2.54 and 3.21; 5-H$_2$)-methine (2.17; 4a-H)-methine proton (4.34; 4-H) and methine (2.17; 4a-H)-methine (4.15; 13b-H)-methylene ones (2.29 and 3.04; 1-H$_2$). The configurations among the 4-H, 4a-H, and 13b-H were deduced to be trans (J_{4-4a}=9.9 Hz) and cis (J_{4a-13b}: small) also based on the coupling constants. The formation of **8** was explained by hydrolysis of ketene acetal moiety of **7**.

These reaction features were explained by the frontier molecular orbital (FMO) analysis[5] using the model compounds;[6] the occupied π-electron energy level of the ene moiety in **2c** shifted upward and both Diels–Alder reactions could be competitive with the ene reaction.

The thermal reaction of **4a** gave the only product **11a** in 76% yield. In the ^{1}H NMR spectrum of **11a**, no signals assigned to olefinic protons were shown and no absorption bands assignable to ester carbonyl were observed in its IR spectrum. The ^{13}C NMR spectra including DEPT measurement of **11a** showed seven sp^3-carbon signals; one methyl (δ=14.9), four methylene (30.2, 50.1, 64.6, and 69.6), and two methine ones (27.5 and 28.6). The ^{1}H–^{13}C and ^{1}H–^{1}H COSY spectra of **11a** elucidated two sets of the alignment of methylene (δ=ca. 4.3; 4-H$_2$)-methine (2.23; 4a-H)-methylene protons (3.18 and 3.37; 5-H$_2$) and methine (2.23; 4a-H)-methine proton (ca. 4.3; 13b-H). The structure of **11a** was deduced to be 6-benzyl-1-cyano-2-ethoxy-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]pyrido[1,2-*a*]pyrimidin-13(4*H*)-one comparing with the proton signal patterns of the similar intramolecular hetero Diels–Alder adducts extensively studied by Tietze and other workers.[7] Although the configuration between the 4a-H and 13b-H in **11a** could not be established



Scheme 2. Mono(ethoxycarbonyl)- **2**, bis(ethoxycarbonyl)- **3**, and cyano(ethoxycarbonyl)-substituted vinyl substrates **4**.



Scheme 3. Thermal reaction of **2** leading to ene products **5** and/or Diels–Alder products **6** and **7**.

due to the signal overlapping of 4-H and 13b-H, it was tentatively assigned to be cis from the similarity to the signal patterns of other cis-annulated products and the results of X-ray single crystal structure analysis of similar hetero Diels–Alder cycloadducts as described later. Similar reaction of 3-[(2-cyano-2-ethoxycarbonyl)vinyl] substrate **4b** and **4c** gave only hetero Diels–Alder adducts **11b** and **11c** in good yields (Scheme 4). Therein, addition of tertiary amines such as triethylamine and diisopropylethylamine to the reaction mixture accelerated the progress of the hetero Diels–Alder reaction (Table 1, runs 7, 9, and 10). Probably, the isomerization between *E*- and *Z*-isomers of **4a**–**4c** could be catalyzed by the tertiary amines and only the *Z*-isomers could perform the hetero Diels–Alder reaction in an *endo* approaching manner leading to products **11**. Especially, the condensation of aldehyde **1c** and ethyl cyanoacetate in ethanol at room temperature afforded an inseparable (1:4) mixture of hetero Diels–Alder adduct **11c** and the desired **4c**.

The competition between the hetero Diels–Alder reaction and the ene reaction similar to that of substrates **2** was also observed in the thermal reaction of 3-[2,2-bis(ethoxycarbonyl)]vinyl substrates **3a** and **3b**; the thermal reaction of **3a** gave azepine **9a**, while the reaction of **3b** gave **9b** and hetero Diels–Alder adduct **10** in ca. 35 and 42% yields, respectively. The configurations of the 4- and 5-position of the azepine ring of **5b**, **5c**, and **9b** could not be established only by their coupling constants, we assigned them to be cis on the basis of the stereochemical strictness of the imine- and carbonyl-ene reactions in this system.[1b] These results are summarized in Schemes 3 and 4 and Table 1.

As described above, strongly electron-withdrawing substituents on the vinyl moiety and an electron-donating one on the alkenylamino moiety changed the reaction feature from the ene reaction to the hetero Diels–Alder reaction. These results suggest that the hetero Diels–Alder reaction proceeds in an inverse electron-demanded manner.[8] The reaction features were also explained by the FMO analysis; the calculation results showed that the frontier π-electron energy levels (π*) of α,β-unsaturated ester carbonyl moieties of **2a**, **3a**, and **4a** were expected to shift downward in the order. The frontier π*-level becomes closer to the frontier π-level and the interaction between the frontier orbitals would be predominantly operated. The reaction features of substrates **2**–**4** would change from the ene reaction to the hetero Diels–Alder reaction.[6]

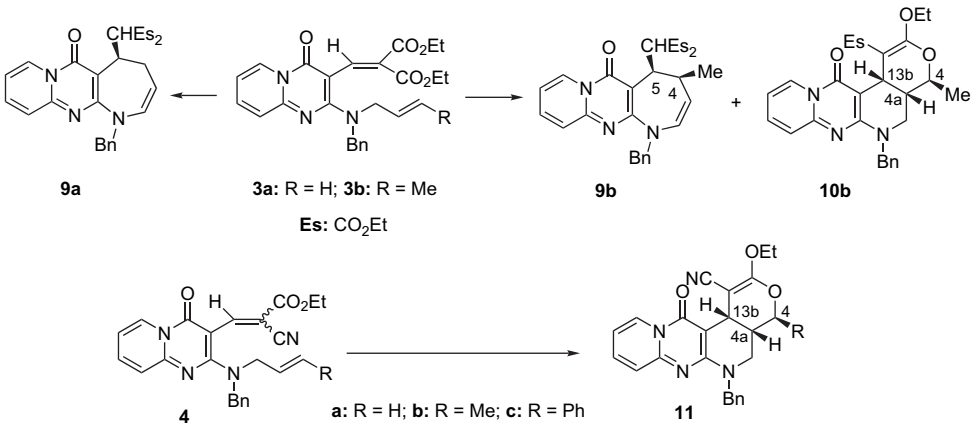
Table 1. Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-(2-substituted or 2,2-disubstituted)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones **2**, **3**, and **4**

Entry	Substrate	Solvent/under reflux	Time (h)	Products/Yield[a] (%)
1	**2a**	Xylene	80	**5a**/75
2	**2b**	Xylene	70	**5b**/80
3	**2c**	Xylene	26	**5c**/35; **6**/35; **8**/11
4	**3a**	Xylene	45	**9a**/73
5	**3b**	Xylene	28	**9b**/ca. 35; **10**/42[b]
6	**4a**	Xylene	24	**11a**/76
7	**4a**	Xylene[c]	24	**11a**/88
8	**4b**	Xylene	24	**11b**/80
9	**4b**	Benzene[d]	30	**11b**/92
10	**4c**[e]	Benzene[d]	15	**11c**/86

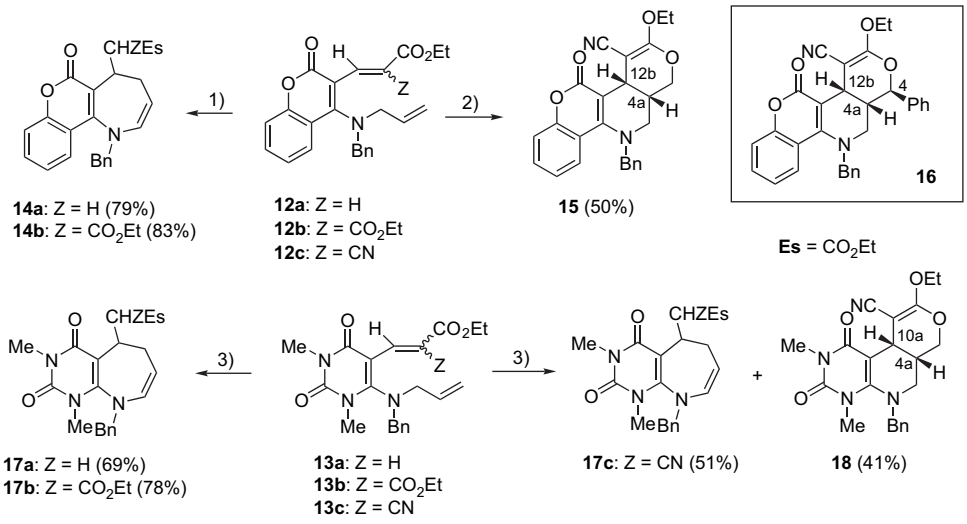
[a] Based on isolated products.
[b] Two other unidentified products were also obtained.
[c] $EtN(i\text{-}Pr)_2$ (1.0 equiv) was added.
[d] NEt_3 (1.0 equiv) was added.
[e] A (4:1) mixture of **4c** and **11c** was used.

2.2. The competitive thermal ene and hetero Diels–Alder reactions in other heterocyclic systems

In order to obtain further information on the reaction features, we examined the similar reactions in other two systems; 4-(*N*-allylbenzylamino)-3-vinyl[1]benzopyran-2(2*H*)-ones **12** and 6-(*N*-allylbenzylamino)-1,3-dimethyl-5-vinylpyrimidine-2,4(1*H*,3*H*)-diones **13** were prepared. The reaction of 2-(ethoxycarbonyl)vinyl **12a** and 2,2-[bis-(ethoxycarbonyl)]vinyl **12b** in refluxing xylene gave the expected ene products **14a** and **14b**. On the other hand, a similar reaction of [2-cyano-2-(ethoxycarbonyl)]vinyl **12c** gave hetero Diels–Alder adduct **15** in a moderate yield along with the unreacted **12c**. Addition of 1,8-diazabicyclo[2.2.2]octane (DABCO™) as a tertiary amine to the reaction mixture did not provide any improvement of the yield of **15**. Fortunately, X-ray single crystal structure analysis[9] was accomplished for products **15** and **16**[10] and, consequently, the ^{1}H NMR spectral assignments concerning the pyran and pyridine ring of the hetero Diels–Alder adducts **15** and **16** were fully accomplished. Finally, the reaction of **13a** and **13b** in refluxing *o*-dichlorobenzene (ODCB) gave ene products **17a** and **17b** in moderate to good yields together with a small amount



Scheme 4. Thermal reaction of **3** and **4** leading to ene products **9** and/or Diels–Alder products **10b** and **11**.



Scheme 5. Reaction of **12** and **13** leading to ene products **14** and **17** and/or hetero Diels–Alder products **15** and **18**. *Reaction conditions*: (1) xylene, reflux, 20 h; (2) xylene, reflux, 36 h; (3) ODCB, reflux, 25 h.

of polymeric products. On the other hand, the similar reaction of **13c** gave ene product **17c** and hetero Diels–Alder adduct **18** (Scheme 5).

3. Conclusions

2-(Ethoxycarbonyl)- and [2-(ethoxycarbonyl)-2-substituted]-vinyl heterocyclic compounds bearing the (alk-2-enyl)amino moiety at the adjacent position performed a competitive 7-(1,4) intramolecular ene reaction and hetero Diels–Alder reaction. The reaction features depended upon the electronic nature of both the substituents of the alkenylamino and the vinyl moieties and we suggested the the FMO analysis should be useful for their understandings.

4. Experimental section

4.1. General

Melting points were measured on a Yamagimoto micro melting point apparatus and are uncorrected. IR spectra were measured on JASCO IR-Report-100 or HORIBA FT-200 spectrophotometer from samples as KBr pellets or NaCl discs. NMR spectra were measured on a JEOL EX-270 spectrometer (270 MHz for ^{1}H and 67.8 MHz for ^{13}C) in deuteriochloroform solutions. Tetramethylsilane was used as internal standard and *J* values are given in hertz. Splitting patterns are indicated as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal; and ov, overlapping signals. Elemental analyses were performed on a Hitachi 026 CHN analyser. All non-aqueous reactions were run under positive pressure of argon or nitrogen. All solvents were dried by standard methods before use. The progress of reactions was monitored by TLC (silica gel 60 F_{254}, Merck). Chromatographic purification was performed with Wakogel C-200 (100–200 mesh, Wako Pure Chemical Industries) and/or silica gel 60 (230–400 mesh, Merck). The starting aldehydes **1a**–**1c**, 4-(*N*-allylbenzylamino)-3-formyl[1]benzopyran-2(2*H*)-one and 6-(*N*-allylbenzylamino)-5-formyl-1,3-dimethylpyrimidin-2,4(1*H*,3*H*)-dione in this study were known.[1]

4.2. Preparation of mono(ethoxycarbonyl)-substituted vinyl compounds 2, 12a, and 13a

Typical procedures. To a solution of aldehyde **1a** (0.32 g, 1.0 mmol) and ethyl (diethylphosphono)acetate (0.27 g, 1.0 mmol) in THF (5 ml), 0.12 g of sodium hydride (50% in mineral oil; 2.5 mmol) was added, and the resultant mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue was extracted with dichloromethane (2×20 ml). The dichloromethane was evaporated to dryness. The residue was subjected to silica-gel column chromatography to afford **2a** (0.18 g, 46%) with hexane/ethyl acetate (3/1) as an eluent.

4.2.1. 2-(*N*-Allylbenzylamino)-3-(2-ethoxycarbonyl)-vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (2a). Yellow crystals from EtOH; mp 155–156 °C; IR (KBr): 1700, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.25 (3H, t, *J*=7.3 Hz, CH_2CH_3), 4.06 (2H, d, *J*=5.6 Hz, –CH_2CH=), 4.18 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.82 (2H, s, CH_2Ph), 5.20–5.31 (2H, ov, =CH_2), 5.99 (1H, m, –CH_2CH=), 6.95 (1H, dd, *J*=6.6, 7.3 Hz, 7-H), 7.16 (1H, d, *J*=15.5 Hz, –CH=CH–Es), 7.26–7.33 (6H, ov, Ph–H and 9-H), 7.62 (1H, dd, *J*=6.6, 7.0 Hz, 8-H), 7.72 (1H, d, *J*=15.5 Hz, –CH=CH–Es), 8.93 (1H, d, *J*=7.3 Hz, 6-H). Anal. Calcd for $C_{23}H_{23}N_3O_3$ (389.4): C, 70.93; H, 5.95; N, 10.79%; found: C, 70.89; H, 5.96; N, 10.74%. This compound was a (19:1) mixture of *E*- and *Z*-isomer; ^{1}H NMR spectral signals due to the *Z*-isomer: 6.76 (d, *J*=11.5 Hz, –CH=CH–Es), 6.88 (7-H), 9.91 (6-H).

4.2.2. 2-[*N*-Benzyl-(*E*)-(but-2-enyl)amino]-3-(2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (2b). Yellow prisms from EtOH; mp 148–149 °C; IR (KBr): 1720, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.27 (3H, t, *J*=7.3 Hz, CH_2CH_3), 1.74 (3H, br d, *J*=4.3 Hz, =CH–*Me*), 3.99 (2H, d, *J*=4.0 Hz, >NCH_2CH=), 4.18 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.81 (2H, s, CH_2Ph), 5.56–5.65 (2H, ov, –CH=CH–Me), 6.94 (1H, dd, *J*=7.0, 7.3 Hz, 7-H), 7.15

(1H, d, J=15.5 Hz, –CH=C*H*–Es), 7.26–7.32 (6H, ov, Ph–H and 9-H), 7.62 (1H, dd, J=5.3, 7.0 Hz, 8-H), 7.70 (1H, d, J=15.5 Hz, –C*H*=CH–Es), 8.94 (1H, br d, J=7.3 Hz, 6-H). Anal. Calcd for $C_{24}H_{25}N_3O_3$ (403.5): C, 71.44; H, 6.24; N, 10.41%; found: C, 71.87; H, 6.37; N, 10.38%.

4.2.3. 2-[*N*-Benzyl-(*E*)-cinnamylamino]-3-(2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (2c). Yellow crystals from EtOH; mp 162–163 °C; IR (KBr): 1700, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.22 (3H, t, J=7.1 Hz, CH_2CH_3), 4.15 (2H, q, J=7.1 Hz, CH_2CH_3), 4.29 (2H, d, J=6.3 Hz, $>NCH_2CH$=), 4.86 (2H, s, CH_2Ph), 6.34 (1H, td, J=6.3, 15.8 Hz, –C*H*=CH–Ph), 6.49 (1H, d, J=15.8 Hz, –CH=C*H*–Ph), 6.97 (1H, dd, J=6.6, 7.3 Hz, 7-H), 7.17 (1H, d, J=15.5 Hz, –CH=C*H*–Es), 7.20–7.40 (11H, ov, Ph–H and 9-H), 7.67 (1H, dd, J=6.6, 7.0 Hz, 8-H), 7.75 (1H, d, J=15.5 Hz, –C*H*=CH–Es), 8.97 (1H, br d, J=7.3 Hz, 6-H). Anal. Calcd for $C_{29}H_{27}N_3O_3$ (465.5): C, 74.82; H, 5.85; N, 9.03%; found: C, 74.66; H, 6.05; N, 9.01%.

4.2.4. 4-(*N*-Allylbenzylamino)-3-(2-ethoxycarbonyl)vinyl[1]benzopyran-2(2*H*)-one (12a). Yellow prisms from EtOH; mp 119–120 °C; IR (KBr): 1720, 1670 cm^{-1}; ^1H NMR ($CDCl_3$): 1.30 (3H, t, J=7.3 Hz, CH_2CH_3), 3.88 (2H, d, J=6.9 Hz, $>NCH_2CH$=), 4.23 (2H, q, J=7.3 Hz, CH_2CH_3), 4.56 (2H, s, CH_2Ph), 5.25 (1H, dd, J=1.3, 17.1 Hz, –CH=CH*H*), 5.36 (1H, dd, J=1.3, 10.2 Hz, –CH=C*H*H), 5.85 (1H, m, –CH_2CH=CH_2), 7.06 (1H, d, J=15.8 Hz, –CH=C*H*–Es), 7.18–7.64 (10H, ov, Ar–H and –C*H*=CH–Es). Anal. Calcd for $C_{24}H_{23}NO_4$ (389.4): C, 74.02; H, 5.95; N, 3.60%; found: C, 73.82; H, 6.21; N, 3.83%.

4.2.5. 6-(*N*-Allylbenzylamino)-5-(2-ethoxycarbonyl)vinyl-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (13a). Colorless crystals from EtOH; mp 124–125 °C; IR (KBr): 1700, 1670, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.27 (3H, t, J=7.3 Hz, CH_2CH_3), 3.34 (3H, s, 1-Me), 3.38 (3H, s, 3-Me), 4.06 (2H, d, J=6.9 Hz, $>NCH_2CH$=), 4.19 (2H, q, J=7.3 Hz, CH_2CH_3), 4.28 (2H, s, CH_2Ph), 5.27–5.40 (2H, ov, –CH=CH_2), 5.84 (1H, m, –C*H*=CH_2), 7.05 (1H, d, J=15.5 Hz, –CH=C*H*–Es), 7.17–7.40 (6H, ov, Ph–H and –C*H*=CH–Es). Anal. Calcd for $C_{21}H_{25}N_3O_4$ (383.4): C, 65.78; H, 6.57; N, 10.96%; found: C, 66.10; H, 6.39; N, 10.69%.

4.3. Preparation of bis(ethoxycarbonyl)-substituted vinyl compounds 3, 12b, and 13b

Typical procedures. A solution of aldehyde **1a** (0.64 g, 2.0 mmol), diethyl malonate (0.30 ml, 2.2 mmol), piperidine (0.40 ml, 4.0 mmol), and acetic acid (0.23 ml, 4.0 mmol) in benzene (10 ml) was refluxed for 12 h. Usual work-up using silica-gel column gave **3a** (0.27 g, 31%) with hexane/ethyl acetate (4/1).

4.3.1. 2-(*N*-Allylbenzylamino)-3-[2,2-bis(ethoxycarbonyl)vinyl]pyrido[1,2-*a*]pyrimidin-4(4*H*)-one (3a). Yellow prisms from EtOH; mp 114–116 °C; IR (KBr): 1710, 1700, 1680 cm^{-1}; ^1H NMR ($CDCl_3$): 1.23, 1.36 (each 3H, each t, J=7.3 Hz, CH_2CH_3), 4.09 (2H, d, J=5.6 Hz, $>NCH_2CH$=), 4.16, 4.36 (each 2H, each d, J=7.3 Hz, CH_2CH_3), 4.84 (2H, s, CH_2Ph), 5.19–5.32 (2H, ov, –CH=CH_2), 5.94 (1H, m, –C*H*=CH_2), 6.92 (1H, dd, J=6.6, 7.3 Hz, 7-H), 7.24–7.36 (6H, ov, Ph–H and 9-H), 7.58 (1H, –C*H*=CEs_2), 7.70 (1H, dd, J=6.0, 6.6 Hz, 8-H), 8.89 (1H, br d, J=7.3 Hz, 6-H). Anal. Calcd for $C_{26}H_{27}N_3O_5$ (461.5): C, 67.66; H, 5.90; N, 9.11%; found: C, 67.75; H, 5.89; N, 9.14%.

4.3.2. 2-[*N*-Benzyl-(*E*)-(but-2-enyl)amino]-3-[2,2-bis(ethoxycarbonyl)vinyl]pyrido[1,2-*a*]pyrimidin-4(4*H*)-one (3b). Yellow prisms from hexane/benzene; mp 132–133 °C; IR (KBr): 1710, 1700, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.24, 1.33 (each 3H, each t, J=7.3 Hz, CH_2CH_3), 1.73 (3H, d, J=4.3 Hz, –CH=CH–*Me*), 4.02 (2H, d, J=4.6 Hz, –CH_2CH=), 4.16, 4.35 (each 2H, each q, J=7.3 Hz, CH_2CH_3), 4.82 (2H, s, CH_2Ph), 5.59–5.64 (2H, ov, –C*H*=C*H*–Me), 6.90 (1H, dd, J=7.0, 7.3 Hz, 7-H), 7.23–7.36 (6H, ov, Ph–H and 9-H), 7.56 (1H, s, –C*H*=CEs_2), 7.62 (1H, dd, J=5.3, 7.0 Hz, 8-H), 8.88 (1H, d, J=7.3 Hz, 6-H). Anal. Calcd for $C_{27}H_{29}N_3O_5$ (475.3): C, 68.19; H, 6.15; N, 8.84%; found: C, 68.02; H, 6.15; N, 8.83%.

4.3.3. 4-(*N*-Allylbenzylamino)-3-[2,2-bis(ethoxycarbonyl)vinyl][1]benzopyran-2(2*H*)-one (12b). Pale yellow crystals from hexane/benzene; mp 108–109 °C; IR (KBr): 1740, 1710, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.29, 1.30 (each 3H, each t, J=7.3 Hz, CH_2CH_3), 3.89 (2H, d, J=6.6 Hz, $>NCH_2CH$=), 4.22–4.34 (4H, ov, CH_2CH_3), 4.58 (2H, s, CH_2Ph), 5.26 (1H, dd, J=1.3, 17.2 Hz, –CH=CH*H*), 5.36 (1H, dd, J=1.3, 10.2 Hz, –CH=C*H*H), 5.85 (1H, m, –CH_2CH=CH_2), 7.19–7.39 (7H, ov, Ar–H), 7.40 (1H, s, 3-C*H*=CEs_2), 7.52–7.62 (2H, ov, Ar–H). Anal. Calcd for $C_{27}H_{27}NO_6$ (461.5): C, 70.27; H, 5.90; N, 3.04%; found: C, 69.82; H, 6.12; N, 3.32%.

4.3.4. 6-(*N*-Allylbenzylamino)-5-[2,2-bis(ethoxycarbonyl)vinyl]-1,3-dimethylpyrimidin-2,4(1*H*,3*H*)-dione (13b). Colorless crystals from EtOH; mp 151–152 °C; IR (KBr): 1720, 1710, 1670 cm^{-1}; ^1H NMR ($CDCl_3$): 1.26, 1.27 (each 3H, each t, J=7.3 Hz, CH_2CH_3), 3.31 (3H, s, 1-Me), 3.33 (3H, s, 3-Me), 3.63 (2H, d, J=6.9 Hz, $>NCH_2CH$=), 4.17–4.34 (6H, ov, CH_2CH_3 and CH_2Ph), 5.27–5.40 (2H, ov, –CH=CH_2), 5.83 (1H, m, –C*H*=CH_2), 7.12 (1H, s, –C*H*=CEs_2), 7.19–7.39 (5H, ov, Ph–H). Anal. Calcd for $C_{24}H_{29}N_3O_6$ (455.5): C, 63.28; H, 6.42; N, 9.22%; found: C, 63.12; H, 6.29; N, 9.23%.

4.4. Preparation of [cyano(ethoxycarbonyl)]-substituted vinyl compounds 4, 12c, and 13c

Typical procedures. A solution of aldehyde **1a** (0.64 g, 2.0 mmol), ethyl cyanoacetate (3 ml, 15.6 mmol), potassium acetate (0.41 g, 4.2 mmol) in EtOH (10 ml) was stirred at room temperature for 6 h. Usual work-up using silica-gel column gave **4a** (0.80 g, 96%) with hexane/ethyl acetate (3/1).

4.4.1. 2-(*N*-Allylbenzylamino)-3-(2-cyano-2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (4a). Yellow paste; IR (KBr): 2200, 1710, 1680, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.33 (3H, t, J=7.3 Hz, CH_2CH_3), 4.11 (2H, d, J=5.6 Hz, $>NCH_2CH$=), 4.29 (2H, q, J=7.3 Hz, CH_2CH_3), 4.85 (2H, s, CH_2Ph), 5.16–5.31 (2H, ov, –CH=CH_2), 5.91 (1H, m, –C*H*=CH_2), 6.98 (1H, dd, J=6.6, 7.3 Hz, 7-H), 7.26–7.37 (6H, ov, Ph–H and 9-H), 7.70 (1H, dd, J=6.6, 7.0 Hz, 8-H), 8.26 (1H, s, –C*H*=C(CN)Es), 8.96 (1H, br d, J=7.3 Hz, 6-H). Anal. Calcd for

$C_{23}H_{22}N_4O_3$ (414.5): C, 69.55; H, 5.35; N, 13.52%; found: C, 69.92; H, 5.51; N, 13.32%. This compound was a (6:1) mixture of *E*- and *Z*-isomer; ^{1}H NMR spectral signal due to the *Z*-isomer: 8.87 (br d, *J*=7.3 Hz, 6-H).

4.4.2. 2-[*N*-Benzyl-(*E*)-(but-2-enyl)amino]-3-(2-cyano-2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (4b). Yellow paste; IR (KBr): 2200, 1720, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.35 (3H, t, *J*=7.3 Hz, CH_2CH_3), 1.71 (3H, d, *J*=5.0 Hz, =CH–*Me*), 4.02 (2H, d, *J*=4.6 Hz, >NCH_2CH=), 4.30 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.83 (2H, s, CH_2Ph), 5.52–5.60 (2H, ov, –CH=CH–), 6.95 (1H, dd, *J*=7.0, 7.3 Hz, 7-H), 7.24–7.36 (6H, ov, Ph–H and 9-H), 7.72 (1H, dd, *J*=5.3, 7.0 Hz, 8-H), 8.25 (1H, s, –CH=C(CN)Es), 8.94 (1H, br d, *J*=7.3 Hz, 6-H). Anal. Calcd for $C_{25}H_{24}N_4O_3$ (428.5): C, 70.07; H, 5.65; N, 13.08%; found: C, 69.65; H, 5.81; N, 12.71%. This compound was a (7:1) mixture of *E*- and *Z*-isomer; ^{1}H NMR spectral signal due to the *Z*-isomer: 8.85 (br d, *J*=7.3 Hz, 6-H).

4.4.3. 2-[*N*-Benzyl-(*E*)-cinnamylamino]-3-(2-cyano-2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-one (4c). This was obtained as an inseparable (4:1) mixture with hetero Diels–Alder product **11c**. Compound **4c**: ^{1}H NMR ($CDCl_3$): 1.28 (3H, t, *J*=7.3 Hz, CH_2CH_3), 4.22 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.31 (2H, d, *J*=6.2 Hz, >NCH_2CH=), 4.85 (2H, s, CH_2Ph), 6.30 (1H, td, *J*=6.2, 15.5 Hz, –CH=CHPh), 6.55 (1H, d, *J*=15.5 Hz, –CH=CHPh), 6.95 (1H, dd, *J*=7.0, 7.3 Hz, 7-H), 7.24–7.37 (11H, ov, Ph–H and 9-H), 7.72 (1H, dd, *J*=5.3, 7.0 Hz, 8-H), 8.28 (1H, s, –CH=C(CN)Es), 8.94 (1H, br d, *J*=7.3 Hz, 6-H).

4.4.4. 4-(*N*-Allylbenzylamino)-3-(2-cyano-2-ethoxycarbonyl)vinyl[1]benzopyran-2(2*H*)-one (12c). Yellow prisms from EtOH; mp 151–152 °C; IR (KBr): 2225, 1740, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.37 (3H, t, *J*=7.3 Hz, CH_2CH_3), 3.98 (2H, d, *J*=5.6 Hz, >NCH_2CH=), 4.34 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.62 (2H, s, CH_2Ph), 5.25–5.42 (2H, ov, –CH=CH_2), 5.85 (1H, m, –CH=CH_2), 7.16–7.67 (9H, ov, Ar–H), 7.95 (1H, s, –CH=C(CN)Es). Anal. Calcd for $C_{25}H_{22}N_2O_4$ (414.4): C, 72.45; H, 5.35; N, 6.76%; found: C, 72.23; H, 5.36; N, 6.80%.

4.4.5. 6-(*N*-Allylbenzylamino)-5-(2-cyano-2-ethoxycarbonyl)vinyl-1,3-dimethylpyrimidin-2,4(1*H*,3*H*)-dione (13c). Pale yellow needles from EtOH; mp 146–147 °C; IR (KBr): 2200, 1710, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.33 (3H, t, *J*=7.3 Hz, CH_2CH_3), 3.41 (3H, s, 1-Me), 3.41 (3H, s, 3-Me), 3.64 (2H, d, *J*=6.9 Hz, >NCH_2CH=), 4.28, 4.31 (each 1H, each d, *J*=13.3 Hz, CH_2Ph), 5.33 (1H, br d, *J*=17.2 Hz, =CH*H*), 5.43 (1H, br d, *J*=10.2 Hz, =CH*H*), 5.82 (1H, m, –CH=CH_2), 7.20–7.39 (5H, ov, Ph–H), 7.62 (1H, s, –CH=C(CN)Es). Anal. Calcd for $C_{22}H_{24}N_4O_4$ (408.4): C, 64.69; H, 5.92; N, 13.72%; found: C, 64.75; H, 5.88; N, 13.51%.

4.5. Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-(2-ethoxycarbonyl)vinylpyrido[1,2-*a*]pyrimidin-4(4*H*)-ones 2

Typical procedures. A solution of **2a** (0.16 g, 0.4 mmol) in dry xylene (10 ml) was deoxygenated by flushing of argon stream for 30 min and refluxed for 80 h. The solvent was evaporated to dryness and the residue was subjected to silica-gel column chromatography with hexane/ethyl acetate (3/1) as an eluent to afford **5a** (0.12 g, 75%).

4.5.1. 1-Benzyl-5-(ethoxycarbonyl)methyl-4,5-dihydropyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (5a). Yellow paste; IR (NaCl): 1730, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.16 (3H, t, *J*=7.3 Hz, CH_2CH_3), 2.32–2.62 (4H, ov, 4-H_2 and 5-CH_2Es), 4.07 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.52 (1H, m, 5-H), 4.90 (1H, m, 3-H), 5.10, 5.20 (each 1H, each d, *J*=15.8 Hz, CH_2Ph), 6.04 (1H, dd, *J*=2.3, 9.9 Hz, 2-H), 6.86 (1H, dd, *J*=6.6, 7.3 Hz, 9-H), 7.21–7.37 (6H, ov, Ph–H and 11-H), 7.49 (1H, dd, *J*=5.0, 7.3 Hz, 10-H), 8.86 (1H, br d, *J*=6.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$): 14.0 (CH_2CH_3), 31.1 (4-C), 31.6 (5-C), 37.8 (5-CH_2CO–), 55.5 (CH_2Ph), 60.0 (OCH_2CH_3), 103.2 (5a-C), 107.1 (3-C), 113.0 (10-C), 124.7 (9-C), 127.0, 127.5, 128.6, 138.8 (Ph–C), 128.3 (8-C), 130.6 (2-C), 135.0 (11-C), 147.1 (12a-C), 157.6, 158.3 (6- and 11a-C), 172.3 (CO_2). Anal. Calcd for $C_{23}H_{23}N_3O_3$ (389.4): C, 70.93; H, 5.95; N, 10.79%; found: C, 70.48; H, 6.12; N, 10.43%.

4.5.2. (4*R,5*S**)-(±)-1-Benzyl-5-(ethoxycarbonyl)methyl-4-methyl-4,5-dihydropyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (5b).** Pale yellow paste; IR (NaCl): 1720, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.05 (3H, d, *J*=6.9 Hz, CH_2CH_3), 1.15 (3H, d, *J*=7.3 Hz, 4-Me), 2.42 (1H, dd, *J*=10.2, 14.5 Hz, >NCHHCO–), 2.53 (1H, dd, *J*=4.6, 14.5 Hz, >NCHHCO–), 2.82 (1H, m, 4-H), 3.97 (2H, q, *J*=6.9 Hz, CH_2CH_3), 4.33 (1H, m, 5-H), 4.54 (1H, br td, *J*=2.1, 10.2 Hz, 3-H), 5.09, 5.26 (each 1H, each d, *J*=15.5 Hz, CH_2Ph), 5.93 (1H, dd, *J*=3.0, 10.2 Hz, 2-H), 6.87 (1H, dd, *J*=6.6, 7.3 Hz, 9-H), 7.23–7.38 (6H, ov, Ph–H and 11-H), 7.50 (1H, dd, *J*=5.0, 7.3 Hz, 10-H), 8.88 (1H, d, *J*=6.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$): 14.0 (CH_2CH_3), 21.2 (4-Me), 33.7 (5-CH_2Es), 35.8 (4-C), 37.1 (5-C), 55.5 (CH_2Ph), 60.0 (OCH_2CH_3), 103.9 (5a-C), 112.4 (3-C), 113.0 (10-C), 124.9 (9-C), 127.1, 127.8, 128.6, 139.0 (Ph–C), 128.0 (8-C), 128.5 (2-C), 135.0 (11-C), 147.3 (12a-C), 157.3 (11a-C), 158.5 (6-C), 173.2 (CO_2). Anal. Calcd for $C_{24}H_{25}N_3O_3$ (403.5): C, 71.44; H, 6.24; N, 10.41%; found: C, 71.08; H, 6.00; N, 10.22%.

4.5.3. (4*R,5*S**)-(±)-1-Benzyl-5-(ethoxycarbonyl)methyl-4-phenyl-4,5-dihydropyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (5c).** Pale yellow prisms from hexane/benzene; mp 157–158 °C; IR (KBr): 1725, 1665, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$): 0.93 (3H, t, *J*=7.3 Hz, CH_2CH_3), 2.33 (1H, dd, *J*=4.6, 15.2 Hz, 5-CHHCO$_2$–), 2.57 (1H, dd, *J*=13.6, 15.2 Hz, 5-CHHCO$_2$–), 3.71–3.86 (2H, ov, CH_2CH_3), 4.05 (1H, br dd, *J*=2.6, 5.9 Hz, 4-H), 4.59 (1H, m, 5-H), 4.96 (1H, td, *J*=2.3, 10.6 Hz, 3-H), 5.04, 5.44 (each 1H, each d, *J*=15.2 Hz, CH_2Ph), 6.20 (1H, dd, *J*=3.0, 10.6 Hz, 2-H), 6.92 (1H, ddd, *J*=1.3, 6.6, 7.0 Hz, 9-H), 7.21–7.51 (11H, ov, Ph–H and 11-H), 7.54 (1H, ddd, *J*=1.0, 7.0, 8.9 Hz, 10-H), 8.93 (1H, dd, *J*=1.0, 6.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$): 13.8 (CH_2CH_3), 32.7 (5-C), 37.8 (5-CH_2CO_2–), 45.6 (6-C), 55.4 (CH_2Ph), 59.9 (OCH_2CH_3), 103.1 (5a-C), 108.5 (3-C), 113.2, 125.0, 126.5, 127.4, 127.8, 128.1, 128.3, 128.5, 130.5, 130.5, 135.2, 138.8, 143.6 (Ph–C and 2-, 8-, 9-, 10- and 11-C), 147.5 (12a-C), 157.9, 158.7 (6- and 11a-C), 172.5 (CO_2). Anal. Calcd for $C_{29}H_{27}N_3O_3$ (465.5): C, 74.82; H, 5.85; N, 8.91%; found: C, 74.52; H, 5.90; N, 8.91%.

4.5.4. (7a*R,13*S**,13a*R**)-(±)-6-Benzyl-13-(ethoxycarbonyl)-6,7,7a,8,13,13a-hexahydrobenzo[*g*]pyrido[1′,2′:1,2]-pyrimido[4,5-*c*]isoquinolin-14(14*H*)-one (6).** Colorless prisms from hexane/benzene; mp 84–86 °C; IR (KBr): 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.22 (3H, t, *J*=7.3 Hz, CH_2CH_3), 2.49 (1H, m, 7a-H), 2.64 (1H, dd, *J*=2.5, 16.6 Hz, 8-H), 3.01–3.14 (2H, ov, 7-H_2), 3.30 (1H, dd, *J*=5.6, 16.6 Hz, 8-H), 3.89 (1H, d, *J*=8.9 Hz [trans], 13-H), 4.01 (1H, ddd, *J*=1.3, 4.6 [cis], 8.9 Hz [trans], 13a-H), 4.23 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.57, 5.29 (each 1H, each d, *J*=15.2 Hz, CH_2Ph), 6.82 (1H, dt, *J*=1.3, 6.9 Hz, 4-H), 7.04–7.33 (10H, ov, Ar–H and 3-H), 7.50 (1H, ddd, *J*=1.3, 6.6, 6.8 Hz, 2-H), 8.89 (1H, dd, *J*=0.7, 6.8 Hz, 1-H); ^{13}C NMR ($CDCl_3$): 14.1 (CH_2CH_3), 29.4 (7a-C), 31.7 (8-C), 33.3 (13a-C), 47.7 (7-C), 49.8 (13-C), 51.1 (CH_2Ph), 61.2 (OCH_2CH_3), 93.4 (13b-C), 112.0 (3-C), 124.2, 126.6, 126.9, 127.2, 127.5, 127.7, 128.6, 128.8, 129.2, 131.6, 133.7, 135.5, 138.2 (Ar–C), 149.5 (5a-C), 156.1, 156.4 (7a- and 14-C), 174.9 (CO_2). Anal. Calcd for $C_{29}H_{27}N_3O_3$ (465.5): C, 74.66; H, 6.05; N, 9.01%; found: C, 74.73; H, 5.89; N, 9.03%.

4.5.5. (4*R,4a*S**,13b*S**)-(±)-6-Benzyl-2-ethoxy-4-phenyl-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]pyrido[1,2-*a*]pyrimidin-13(4*H*)-one (7).** This compound could not be isolated as a pure form from the reaction mixture and was converted to **8** during column chromatography on silica gel; ^1H NMR ($CDCl_3$): 1.34 (t, *J*=7.1 Hz, CH_2CH_3), 3.78 (s, 1-H), 4.15 (q, *J*=7.1 Hz, CH_2CH_3).

4.5.6. (4*R,4a*S**,13b*R**)-(±)-6-Benzyl-4-phenyl-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]pyrido[1,2-*a*]pyrimidine-2,13(1*H*,4*H*)-dione (8).** Yellow prisms from ethyl acetate; mp 72–73 °C; IR (KBr): 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 2.17 (1H, m, 4a-H), 2.29 (1H, dd, *J*=10.9, 15.5 Hz, 1-H), 2.57 (1H, dd, *J*=2.0, 13.5 Hz, 5-H), 3.04 (1H, dd, *J*=4.0, 15.5 Hz, 1-H), 4.12–4.18 (2H, ov, C*H*HPh and 13b-H), 4.34 (1H, d, *J*=9.9 Hz, 4-H), 5.33 (1H, d, *J*=14.9 Hz, CH*H*Ph), 6.89 (1H, dt, *J*=1.7, 6.9 Hz, 10-H), 7.11–7.32 (11H, ov, Ph–H and 8-H), 7.56 (1H, ddd, *J*=1.7, 6.9, 8.9 Hz, 9-H), 8.91 (1H, br d, *J*=6.9 Hz, 11-H); ^{13}C NMR ($CDCl_3$): 29.7 (13b-C), 38.8 (1-C), 42.4 (4a-C), 43.7 (5-C), 51.7 (CH_2Ph), 74.2 (4-C), 90.9 (13a-C), 112.31 (10-C), 126.7, 127.3, 127.4, 127.9, 128.2, 128.4, 128.5, 128.7, 135.5 (Ph–C and 8- and 9-C), 135.6 (11-C), 142.9 (6a-C), 149.3 (7a-C), 156.8 (13-C), 172.8 (2-C). Anal. Calcd for $C_{27}H_{23}N_3O_3$ (437.5): C, 74.12; H, 5.30; N, 9.61%; found: C, 74.33; H, 5.18; N, 9.78%.

4.6. Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-[2,2-bis(ethoxycarbonyl)vinyl]pyrido[1,2-*a*]pyrimidin-4(4*H*)-ones 3

Typical procedures. A deoxygenated solution of **3a** (0.18 g, 0.4 mmol) in xylene (10 ml) was refluxed for 40 h. The solvent was evaporated to dryness and the residue was subjected to silica-gel column chromatography with hexane/ethyl acetate (3/1) as an eluent to afford **9a** (0.16 g, 89%).

4.6.1. 1-Benzyl-5-[2,2-bis(ethoxycarbonyl)methyl]-4,5-dihydropyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (9a). Pale yellow paste; IR (NaCl): 1740, 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 0.91, 1.27 (each 3H, each t, *J*=7.3 Hz, CH_2CH_3), 2.57 (2H, ov, 4-H_2), 3.80–3.97 (3H, ov, 5-C*H*Es_2 and CH_2CH_3), 4.22 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.76–4.86 (2H, ov, 3- and 5-H), 5.10, 5.23 (each 1H, each d, *J*=15.2 Hz, CH_2Ph), 6.02 (1H, dd, *J*=1.3, 9.6 Hz, 2-H), 6.89 (1H, dd, *J*=6.6, 8.3 Hz, 9-H), 7.23–7.42 (6H, ov, Ph–H and 11-H), 7.53 (1H, dd, *J*=5.0, 8.3 Hz, 10-H), 8.88 (1H, br d, *J*=6.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$): 13.6, 14.1 (CH_2CH_3), 30.2 (4-C), 33.9 (5-C), 53.8 (5-*C*HEs_2), 55.6 (CH_2Ph), 60.9, 61.2 (OCH_2CH_3), 101.5 (5a-C), 105.6 (3-C), 113.1 (10-C), 124.9 (9-C), 127.1, 127.8×2, 138.8 (Ph–C), 128.4 (8-C), 130.3 (2-C), 135.4 (11-C), 147.5 (12a-C), 158.5 (11a-C), 158.5 (6-C), 168.4, 168.5 (CO_2). Anal. Calcd for $C_{26}H_{27}N_3O_5$ (461.5): C, 67.67; H, 5.90; N, 9.10%; found: C, 67.86; H, 6.07; N, 8.75%.

4.6.2. (4*R,5*R**)-(±)-1-Benzyl-5-[2,2-bis(ethoxycarbonyl)methyl]-4-methyl-4,5-dihydropyrido[1′,2′:1,2]pyrimido[4,5-*b*]azepin-6(1*H*)-one (9b).** This compound was contaminated by other unidentified products and could not be isolated as a pure form. The structure was speculated on the basis of its ^1H NMR spectral data; ^1H NMR ($CDCl_3$): 1.08 (3H, d, *J*=7.3 Hz, 4-Me), 1.29 (6H, t, *J*=7.2 Hz, CH_2CH_3), 2.89 (1H, m, 4-H), 3.80–3.85 (2H, ov, 5-C*H*Es_2 and 5-H), 4.22 (4H, q, *J*=7.2 Hz, CH_2CH_3), 4.58 (1H, br d, *J*=9.9 Hz, 3-H), 4.81, 5.43 (each 1H, each d, *J*=15.5 Hz, CH_2Ph), 5.99 (1H, dd, *J*=0.5, 9.9 Hz, 2-H), 6.88 (1H, dt, *J*=0.7, 7.3 Hz, 9-H), 7.21–7.54 (7H, ov, Ph–H and 10- and 11-H), 8.88 (1H, dd, *J*=0.6, 7.3 Hz, 8-H).

4.6.3. (4*R,4a*R**,13b*S**)-(±)-6-Benzyl-2-ethoxy-1-(ethoxycarbonyl)-4-methyl-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]-pyrido[2,3-*d*]pyrido[1,2-*a*]pyrimidin-13(4*H*)-one (10b).** Colorless paste; IR (NaCl): 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$): 1.16 (6H, t, *J*=7.3 Hz, CH_2CH_3), 1.65 (3H, *J*=6.3 Hz, 4-Me), 2.22 (1H, dddd, *J*=2.0, 4.0, 7.6, 10.3 Hz, 4a-H), 3.31 (1H, dd, *J*=3.6, 13.9 Hz, 5-H), 3.71–3.81 (2H, ov, 5- and 13b-H), 3.99–4.15 (5H, ov, 4-H and CH_2CH_3), 4.65, 5.33 (each 1H, each d, *J*=14.8 Hz, CH_2Ph), 6.84 (1H, dd, *J*=7.3, 8.0 Hz, 10-H), 7.25–7.36 (6H, ov, Ph–H and 8-H), 7.54 (1H, dd, *J*=6.6, 8.0 Hz, 9-H), 8.81 (1H, d, *J*=7.3 Hz, 11-H); ^{13}C NMR ($CDCl_3$): 13.8, 13.9 (CH_2CH_3), 23.2 (4-Me), 33.4 (13b-C), 41.4 (4a-C), 44.7 (5-C), 51.5 (CH_2Ph), 55.5 (1-C), 58.7 (4-C), 61.2, 61.5 (OCH_2CH_3), 87.0 (13a-C), 112.3 (10-C), 124.3 (8-C), 127.3 (11-C), 127.4, 127.9, 128.5, 137.8 (Ph–C), 135.9 (9-C), 149.5 (6a-C), 156.6, 156.7 (7a- and 13-C), 168.0 (2-C), 168.3 (CO_2). Anal. Calcd for $C_{27}H_{29}N_3O_5$ (475.3): C, 68.19; H, 6.15; N, 8.84%; found: C, 67.89; H, 6.01; N, 8.60%.

4.7. Thermal reaction of 2-[*N*-(alk-2-enyl)benzylamino]-3-[2-cyano-2-(ethoxycarbonyl)vinyl]pyrido[1,2-*a*]pyrimidin-4(4*H*)-ones 4

Typical procedures. A deoxygenated solution of **4a** (0.26 g, 0.6 mmol) in xylene (10 ml) was refluxed for 24 h. The solvent was evaporated to dryness and the residue was subjected to silica-gel column chromatography with hexane/ethyl acetate (3/1) as an eluent to afford **11a** (0.20 g, 77%).

4.7.1. (4a*R,13b*R**)-(±)-6-Benzyl-1-cyano-2-ethoxy-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]pyrido[1,2-*a*]-pyrimidin-13(4*H*)-one (11a).** Yellow plates from EtOH; mp 211–212 °C; IR (KBr): 2250, 1670 cm^{-1};

^{1}H NMR ($CDCl_3$): 1.25 (3H, t, J=7.3 Hz, CH_2CH_3), 2.23 (1H, m, 4a-H), 3.18 (1H, ddd, J=1.3, 5.0, 12.5 Hz, 5-H), 3.37 (1H, dd, J=12.2, 12.5 Hz, 5-H), 4.12 (2H, q, J=7.3 Hz, CH_2CH_3), 4.25–4.39 (3H, ov, 4-H_2 and 13b-H), 4.70, 5.27 (each 1H, each d, J=15.2 Hz, CH_2Ph), 6.85 (1H, dd, J=5.6, 7.0 Hz, 10-H), 7.20–7.37 (6H, ov, Ph–H and 8-H), 7.54 (1H, dd, J=5.6, 7.2 Hz, 9-H), 8.95 (1H, d, J=7.0 Hz, 11-H); ^{13}C NMR ($CDCl_3$): 14.9 (CH_2CH_3), 27.5 (13b-C), 28.6 (4a-C), 43.8 (5-C), 51.0 (CH_2Ph), 64.6 (OCH_2CH_3), 65.2 (1-C), 69.6 (4-C), 89.4 (13a-C), 112.4 (9-C), 118.5 (CN), 124.1 (10-C), 127.4, 127.6, 128.7, 137.8 (Ph–C), 128.2 (11-C), 136.1 (8-C), 149.8 (6a-C), 156.2 (7a-C), 157.2 (13-C), 165.4 (2-C). Anal. Calcd for $C_{24}H_{22}N_4O_3$ (414.5): C, 69.55; H, 5.35; N, 13.52%; found: C, 69.78; H, 5.43; N, 13.52%.

4.7.2. (4*R,4a*R**,13b*R**)-(±)-6-Benzyl-1-cyano-2-ethoxy-4-methyl-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]-pyrido[1,2-*a*]pyrimidin-13(4*H*)-one (11b).** Yellow needles from EtOH; mp 203–204 °C; IR (KBr): 2200, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.25 (3H, t, J=7.3 Hz, CH_2CH_3), 1.44 (3H, d, J=6.6 Hz, 4-Me), 1.98 (1H, m, 4a-H), 3.12 (1H, dd, J=5.0, 12.5 Hz, 5-H), 3.25 (1H, br t, J=12.5 Hz, 5-H), 4.10 (2H, q, J=7.3 Hz, CH_2CH_3), 4.30 (1H, d, J=5.0 Hz [cis], 13b-H), 4.46 (1H, dq, J=1.3, 6.6 Hz, 4-H), 4.68, 5.27 (each 1H, each d, J=15.2 Hz, CH_2Ph), 6.86 (1H, dd, J=5.6, 7.3 Hz, 10-H), 6.83–7.37 (6H, ov, Ph–H and 8-H), 7.54 (1H, br dd, J=5.6, 7.6 Hz, 9-H), 8.97 (1H, br d, J=7.3 Hz, 11-H); ^{13}C NMR ($CDCl_3$): 14.8 (CH_2CH_3), 18.8 (4-Me), 25.1 (13b-C), 31.7 (4a-C), 45.2 (5-C), 50.9 (CH_2Ph), 63.9 (1-C), 64.3 (OCH_2CH_3), 75.9 (4-C), 89.0 (13a-C), 112.3 (9-C), 118.5 (CN), 124.1 (10-C), 127.3, 127.5, 128.6, 137.8 (Ph–C), 128.1 (11-C), 136.0 (8-C), 149.8 (6a-C), 156.4 (7a-C), 157.2 (13-C), 161.9 (2-C). Anal. Calcd for $C_{25}H_{24}N_4O_3$ (428.5): C, 70.07; H, 5.65; N, 13.08%; found: C, 70.00; H, 5.71; N, 13.02%.

4.7.3. (4*R,4a*S**,13b*S**)-(±)-6-Benzyl-1-cyano-2-ethoxy-4-phenyl-4a,5,6,13b-tetrahydropyrano[4′,3′:4,5]pyrido[2,3-*d*]pyrido[1,2-*a*]pyrimidin-13(4*H*)-one (11c).** Yellow prisms from EtOH; mp 220–221 °C; IR (KBr): 2200, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.23 (3H, t, J=7.3 Hz, CH_2CH_3), 2.36 (1H, m, 4a-H), 3.30–3.46 (2H, ov, 5-H_2), 3.97 (1H, d, J=4.6 Hz [cis], 13b-H), 4.24 (2H, q, J=7.3 Hz, CH_2CH_3), 4.75, 5.28 (each 1H, each d, J=15.2 Hz, CH_2Ph), 5.36 (1H, br s, 4-H), 6.83 (1H, dd, J=6.6, 7.2 Hz, 10-H), 7.19–7.42 (11H, ov, Ph–H and 8-H), 7.52 (1H, dd, J=5.0, 7.2 Hz, 9-H), 8.90 (1H, d, J=6.6 Hz, 11-H); ^{13}C NMR ($CDCl_3$): 15.0 (CH_2CH_3), 25.1 (13b-C), 33.4 (4a-C), 45.8 (5-C), 51.1 (CH_2Ph), 64.7 (OCH_2CH_3), 65.3 (1-C), 80.6 (4-C), 89.3 (13a-C), 112.4 (9-C), 118.3 (CN), 124.1 (10-C), 124.6, 124.7, 127.4, 127.6, 128.5, 128.7, 129.0, 137.8, 137.9 (Ph–C), 128.1 (11-C), 136.1 (8-C), 149.8 (6a-C), 156.5 (7a-C), 157.0 (13-C), 162.7 (2-C). Anal. Calcd for $C_{30}H_{26}N_4O_3$ (490.5): C, 73.45; H, 5.34; N, 11.42%; found: C, 73.11; H, 5.20; N, 11.36%.

4.8. Compounds 14a, 14b, and 15

Thermal reaction of **12a** and **12b** gave ene products **14a** and **14b**, while reaction of **12c** afforded hetero Diels–Alder product **15**.

4.8.1. 1-Benzyl-5-(ethoxycarbonyl)methyl-6-oxo-4,5-dihydro[1]benzopyrano[4,3-*b*]azepin-6(1*H*)-one (14a). Yellow needles from EtOH; mp 146–147 °C; IR (KBr): 1720, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.21 (3H, t, J=7.3 Hz, CH_2CH_3), 2.02–2.08 (2H, ov, 5-CH_2Es), 2.22 (1H, ddd, J=4.3, 7.6, 17.2 Hz, 4-H), 2.45 (1H, ddd, J=2.9, 5.6, 17.2 Hz, 4-H), 4.07 (2H, q, J=7.3 Hz, CH_2CH_3), 4.13 (1H, m, 5-H), 4.59, 4.87 (each 1H, each d, J=14.5 Hz, CH_2Ph), 4.71 (1H, ddd, J=2.9, 4.3, 9.9 Hz, 3-H), 6.11 (1H, dd, J=2.0, 9.9 Hz, 2-H), 7.19–7.73 (9H, ov, Ph–H); ^{13}C NMR ($CDCl_3$): 14.1 (CH_2CH_3), 30.8 (4-C), 33.1 (5-C), 36.9 (5-CH_2Es), 60.1, 60.2 (CH_2Ph and OCH_2CH_3), 105.8 (5a-C), 117.4 (11b-C), 117.7, 121.6, 123.5×2, 125.2, 128.3, 128.8×2, 130.7, 136.4, 152.4, 152.9 (Ar–C), 162.7 (6-C), 172.1 (CO_2). Anal. Calcd for $C_{24}H_{23}NO_4$ (389.4): C, 74.02; H, 5.95; N, 3.60%; found: C, 74.28; H, 6.03; N, 3.49%.

4.8.2. 1-Benzyl-5-[bis(ethoxycarbonyl)methyl]-4,5-dihydro[1]benzopyrano[4,3-*b*]azepin-6(1*H*)-one (14b). Yellow needles from EtOH; mp 178–179 °C; IR (KBr): 1740, 1710, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.19, 1.22 (each 3H, each t, J=7.3 Hz, CH_2CH_3), 2.35 (1H, ddd, J=4.6, 6.6, 17.5 Hz, 4-H), 2.50 (1H, dd, J=3.0, 17.5 Hz, 4-H), 3.63 (1H, d, J=12.2 Hz, 5-C*H*Es$_2$), 4.00–4.20 (4H, ov, CH_2CH_3), 4.46 (1H, m, 5-H), 4.69 (1H, dd, J=3.0, 9.9 Hz, 3-H), 4.76, 4.82 (each 1H, each d, J=14.5 Hz, CH_2Ph), 6.13 (1H, dd, J=1.3, 9.9 Hz, 2-H), 7.15–7.75 (9H, ov, Ar–H); ^{13}C NMR ($CDCl_3$): 13.9, 14.1 (CH_2CH_3), 29.5 (4-C), 36.2 (5-C), 53.5 (5-*C*HEs$_2$), 59.5 (CH_2Ph), 61.2, 61.4 (OCH_2CH_3), 105.4 (5a-C), 117.6 (11b-C), 117.7, 119.7, 123.5, 124.7, 128.1, 129.0, 130.9, 136.3, 152.8, 152.9 (Ar–C), 162.6 (6-C), 168.1, 168.5 (CO_2). Anal. Calcd for $C_{27}H_{27}NO_6$ (389.4): C, 70.27; H, 5.90; N, 3.03%; found: C, 70.15; H, 5.99; N, 2.78%.

4.8.3. (4a*R,12b*R**)-(±)-6-Benzyl-1-cyano-2-ethoxy-4a,5,6,12b-tetrahydro[1]benzopyrano[4,3-*b*]pyrano[4,3-*d*]pyridin-12(4*H*)-one (15).** Yellow prisms from EtOH; mp 231–232 °C; IR (KBr): 2200, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.27 (3H, t, J=7.3 Hz, CH_2CH_3), 2.14 (1H, m, 4a-H), 3.14 (1H, dd, J=4.0, 12.2 Hz, 5-H), 3.26 (1H, br t, J=12.2 Hz, 5-H), 4.01–4.18 (3H, ov, 12b-H and CH_2CH_3), 4.29 (1H, dd, J=1.7, 11.6 Hz, 4-H), 4.42 (1H, dd, J=2.6, 11.6 Hz, 4-H), 4.62, 4.82 (each 1H, each d, J=16.8 Hz, CH_2Ph), 7.05–7.57 (9H, ov, Ar–H); ^{13}C NMR ($CDCl_3$): 14.9 (CH_2CH_3), 26.1 (12b-C), 29.3 (4a-C), 46.7 (5-C), 59.0 (CH_2Ph), 64.6, 64.7 (1-C and OCH_2CH_3), 69.5 (4-C), 104.4 (12a-C), 115.8 (6a-C), 118.0 (CN), 118.2, 123.4, 124.3, 126.8, 128.0, 129.3, 131.3, 136.4, 153.3, 153.6 (Ar–C), 161.8 (12-C), 163.7 (2-C). Anal. Calcd for $C_{25}H_{22}N_2O_4$ (414.4): C, 72.45; H, 5.35; N, 6.76%; found: C, 72.27; H, 5.46; N, 6.44%. The structure of **15** was confirmed by X-ray single crystal structure analysis.[9]

4.9. Compounds 17a, 17b, 17c, and 18

Thermal reaction of **13a** and **13b** gave ene products **17a** and **17b**, on the other hand **13c** gave ene product **17c** and hetero Diels–Alder product **18**.

4.9.1. 9-Benzyl-5-(ethoxycarbonyl)methyl-1,3-dimethyl-6,9-dihydro-1*H*-pyrimido[4,5-*b*]azepin-2,4(3*H*,5*H*)-dione (17a). Colorless needles from EtOH; mp 146–147 °C;

IR (KBr): 1730, 1640, 1620 cm^{-1}; ^1H NMR ($CDCl_3$): 1.18 (3H, t, J=7.3 Hz, CH_2CH_3), 1.80 (2H, br s, 5-CH_2Es), 2.13 (1H, ddd, J=4.3, 5.6, 17.2 Hz, 6-H), 2.32 (1H, br d, J=17.2 Hz, 6-H), 3.37 (3H, s, 1-Me), 3.46 (3H, s, 3-Me), 3.94–4.03 (3H, ov, 5-H and CH_2CH_3), 4.23, 4.34 (each 1H, each d, J=14.2 Hz, CH_2Ph), 4.71 (1H, m, 7-H), 5.90 (1H, br d, J=9.9 Hz, 8-H), 7.22–7.38 (5H, ov, Ph–H); ^{13}C NMR ($CDCl_3$): 14.1 (CH_2CH_3), 28.6 (1-Me), 29.0 (6-C), 31.1 (5-C), 35.5 (3-Me), 36.5 (5-CH_2Es), 58.4 (CH_2Ph), 60.0 (OCH_2CH_3), 107.6 (4a-C), 108.9 (7-C), 128.7, 128.9, 129.3, 135.1 (Ph–C), 129.0 (2-C), 151.0 (9a-C), 153.2 (2-C), 162.9 (4-C), 172.3 (CO_2). Anal. Calcd for $C_{21}H_{25}N_3O_4$ (383.4): C, 65.78; H, 6.57; N, 10.96%; found: C, 65.57; H, 6.65; N, 10.63%.

4.9.2. 9-Benzyl-5-[bis(ethoxycarbonyl)methyl]-1,3-dimethyl-6,9-dihydro-1*H*-pyrimido[4,5-*b*]azepin-2,4(3*H*,5*H*)-dione (17b). Colorless needles from hexane/benzene; mp 159–160 °C; IR (KBr): 1740, 1715, 1645 cm^{-1}; ^1H NMR ($CDCl_3$): 1.14–1.21 (6H, ov, CH_2CH_3), 2.21 (1H, br td, J=4.6, 17.8 Hz, 6-H), 2.30 (1H, br d, J=17.8 Hz, 6-H), 3.29 (1H, m, 5-H), 3.35 (3H, s, 1-Me), 3.44 (3H, s, 3-Me), 3.99–4.13 (5H, ov, CH_2CH_3 and 5-CHEs$_2$), 4.32, 4.40 (each 1H, each d, J=14.2 Hz, 9-CH_2Ph), 4.71 (1H, m, 7-H), 5.92 (1H, br d, J=9.9 Hz, 8-H), 7.36 (5H, ov, Ph–H); ^{13}C NMR ($CDCl_3$): 13.8, 14.0 (CH_2CH_3), 28.6 (1-Me), 29.5 (6-C), 32.2 (5-C), 35.4 (3-Me), 52.9 (5-CHEs$_2$), 57.8 (CH_2Ph), 61.0, 61.1 (OCH_2CH_3), 106.9 (4a- and 7-C), 128.4, 128.8, 128.9, 129.1, 135.0 (Ph–C and 8-C), 151.2 (9a-C), 153.1 (2-C), 162.9 (4-C), 168.3 (CO_2). Anal. Calcd for $C_{24}H_{29}N_3O_6$ (383.4): C, 63.28; H, 6.37; N, 9.21%; found: C, 63.19; H, 6.37; N, 9.21%.

4.9.3. 9-Benzyl-5-[cyano(ethoxycarbonyl)methyl]-1,3-dimethyl-6,9-dihydro-1*H*-pyrimido[4,5-*b*]azepin-2,4(3*H*,5*H*)-dione (17c). Colorless needles from EtOH; mp 166–167 °C; IR (KBr): 2250, 1730, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): 1.34 (3H, t, J=6.9 Hz, CH_2CH_3), 2.16 (1H, dd, J=8.9, 14.9 Hz, 6-H), 2.56 (1H, d, J=13.9 Hz, 5-H), 2.90 (1H, ddd, J=1.3, 8.6, 14.9 Hz, 6-H), 3.25 (1H, d, J=13.9 Hz, 5-CH(CN)Es), 3.30 (3H, s, 1-Me), 3.52 (3H, s, 3-Me), 4.11–4.39 (5H, ov, 7-H and CH_2CH_3 and CH_2Ph), 6.12 (1H, d, J=9.9 Hz, 8-H), 7.13–7.36 (5H, ov, Ph–H); ^{13}C NMR ($CDCl_3$): 13.8 (CH_2CH_3), 27.5 (6-C), 28.5 (1-Me), 31.5 (5-C), 34.0 (3-Me), 38.4 (5-CH(CN)Es), 59.7 (CH_2Ph), 63.1 (OCH_2CH_3), 95.6 (7-C), 101.3 (4a-C), 119.9 (CN), 128.3, 129.0, 129.3, 135.0 (Ph–C), 135.5 (8-C), 151.4 (9a-C), 152.3 (2-C), 162.1 (4-C), 167.7 (CO_2). Anal. Calcd for $C_{16}H_{24}N_4O_4$ (408.5): C, 64.69; H, 5.92; N, 13.72%; found: C, 64.58; H, 6.01; N, 13.64%. In the ^1H NMR spectrum of the crude reaction mixture, signals due to another diastereomer were observed, however, the isomer could not be isolated by chromatographic purification: 1.29 (t, J=7.3 Hz, CH_2CH_3), 6.03 (d, J=9.9 Hz, 8-H).

4.9.4. (6a*R,10a*R**)-(±)-5-Benzyl-10-cyano-9-ethoxy-2,4-dimethyl-4,5,6,6a,7,10a-hexahydropyrano[3′,4′:6,5]pyrido[3,4-*d*]pyrimidin-1,3(2*H*)-dione (18).** Yellow prisms from EtOH; mp 115–116 °C; IR (KBr): 2200, 1690, 1640 cm^{-1}; ^1H NMR ($CDCl_3$): 1.27 (3H, t, J=6.9 Hz, CH_2CH_3), 1.86 (1H, m, 6a-H), 3.03 (1H, dd, J=2.3, 13.5 Hz, 6-H), 3.18 (1H, dd, J=12.5, 13.5 Hz, 6-H), 3.38, 3.39 (each 3H, each s, 2- and 4-Me), 3.94 (1H, d, J=4.6 Hz [cis], 10a-H), 4.04–4.37 (6H, ov, 4-H and CH_2CH_3 and CH_2Ph), 7.26–7.45 (5H, ov, Ph–H); ^{13}C NMR ($CDCl_3$): 14.9 (CH_2CH_3), 25.2 (4-Me), 28.2 (10a-C), 28.6 (6a-C), 34.3 (2-Me), 46.3 (6-C), 57.2 (CH_2Ph), 64.6 (OCH_2CH_3), 64.8 (10-C), 69.3 (7-C), 96.6 (10b-C), 118.5 (CN), 126.9, 128.2, 129.2, 135.2 (Ph–C), 152.6 (4a-C), 154.0 (3-C), 162.2 (1-C), 163.9 (CO_2). Anal. Calcd for $C_{22}H_{24}N_4O_4$ (408.4): C, 64.69; H, 5.92; N, 13.72%; found: C, 64.41; H, 5.86; N, 13.47%.

References and notes

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3. The desired vinyl compounds **3a**, **3b**, **12b**, and **13b** in this study were also obtained by utilizing other dehydrating conditions, such as in THF at room temperature in the presence of titanium tetrachloride or in acetic anhydride in the presence of zinc dichloride at 80 °C. In some cases, however, tetrahydropyridine derivatives were formed as major products. Details of the tetrahydropyridine synthesis will be described elsewhere.
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6. Preliminary calculations were made using the *N*-methyl substrates instead of *N*-benzyl ones **2**, **3**, **4**, **12**, and **13** in order to avoid conformational and computational complexities by PM3 method[11] with the standard parameters as implemented in a MOPAC program[12] (version 6.00) on the VAX 4000 system. π-Electron energy levels were examined downward from the HOMO and the levels possessing the coefficients at both the carbon atoms of the ene moieties were adopted as the frontier orbitals (π). The similar treatments (examination of the π*-electron levels upward from LUMO) were performed for the α,β-unsaturated ester carbonyl moieties and adopted as the frontier orbitals (π*). Although the substituents on the ene and the α,β-unsaturated ester moieties effected on the both frontier orbitals (π and π*), the substituents on the ene moieties effected predominantly on π and the substituents on the vinyl moieties did on π* as expected. When the energy differences (ΔE) between the frontier orbitals (π* and π) of the model substrates became less than 9.7 eV, the reaction features of the actual substrates **2**, **3**, **4**, **12**, and **13** changed from the ene reactions to the hetero Diels–Alder reactions. In order to perform further discussion on the reaction mechanism, more precise calculations on the energy levels and the transition states are now under progress and the details will be reported elsewhere.

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9. Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-101213 for compound **15** and CCDC-101214 for compound **16**. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
10. Similar condensation of 4-[*N*-benzyl-(*E*)-cinnamylamino]-3-formyl[1]benzopyran-2(2*H*)-one with ethyl cyanoacetate in EtOH at room temperature for 5 h gave not the desired vinyl compound but hetero Diels–Alder product **16** (86%).
(4R,4aS*,12bS*)-(±)-6-Benzyl-1-cyano-2-ethoxy-4-phenyl-4a,5,6,12b-tetrahydro[1]benzopyrano[4,3-b]pyrano[4,3-d]-pyridin-12(4H)-one (**16**)*: yellow prisms from EtOH; mp 223–224 °C; IR (KBr): 2190, 1690 cm^{-1}; ^1H NMR ($CDCl_3$): 1.34 (3H, t, *J*=6.9 Hz, CH_2CH_3), 2.20 (1H, m, 4a-H), 3.28–3.34 (2H, ov, 5-H_2), 3.72 (1H, d, *J*=4.3 Hz [cis], 12b-H), 4.23 (2H, q, *J*=6.9 Hz, CH_2CH_3), 4.71, 4.80 (each 1H, each d, *J*=16.8 Hz, CH_2Ph), 5.37 (1H, br s, 4-H), 7.07–7.65 (9H, ov, Ar–H); ^{13}C NMR ($CDCl_3$): 15.0 (CH_2CH_3), 25.7 (12b-C), 32.1 (4a-C), 48.5 (5-C), 59.0 (CH_2Ph), 64.8 (1-C), 64.9 (OCH_2CH_3), 80.8 (4-C), 104.3 (12a-C), 115.6 (6a-C), 118.0 (CN), 118.1, 123.4, 124.3, 124.4, 127.0, 128.1, 128.7, 129.2, 129.3, 131.3, 136.3, 137.9, 153.3 (Ar–C), 154.1×2 (6b- and 10a-C), 161.7 (12-C), 162.8 (2-C); *m/z*: 490 (M^+). Anal. Calcd for $C_{31}H_{26}N_2O_4$ (490.5): C, 75.90; H, 5.34; N, 5.71%; found: C, 76.12; H, 5.32; N, 5.76%. The structure of **16** was confirmed by X-ray single crystal structure analysis.[9]
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