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A RADICAL SYNTHETIC APPROACH TO THE NEW POTENTIALLY BIOACTIVE PYRIMIDINONES[§]

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Abstract - 2-Chloromethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one was shown to react with various nitronate or malonate anions under mild conditions to give potentially bioactive nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. Extension to other anions centred on *S* or *O* atom allows to generalize this synthetic procedure.

Wagner[1] in 1977 has described the activity of 3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one derivatives against *Trichomonas foetus* and *Entamoeba histolytica*. Satti[2] has reported a good activity of some pyrido[1,2-*a*]pyrimidines against *Leishmania donovani* in 1993. Accumulating interest in these heterocycles was derived from their broad range of useful pharmacological properties, e.g. antidepressant, antihypertensive, analgetic, antiinflammatory, cytoprotective, bronchodilatory, antithrombotic, antiallergic and antiatherosclerotic activities.[3] Since then, an increasing number of pharmaceutical companies[4] have investigated the pharmacological actions of various 4*H*-pyrido[1,2-*a*]pyrimidin-4-one compounds, probably due to their favorable properties: they have relatively low toxicities, and in general they possess good pharmacokinetic properties.

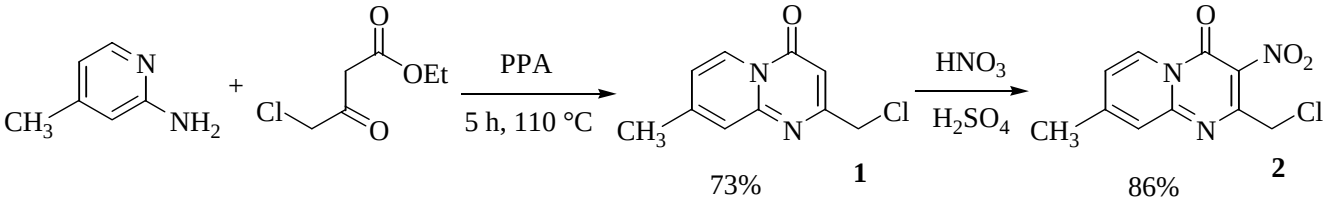
On the other hand, our research investigations into the electron transfer reactions have started in the mid

[§] This paper is dedicated to the memory of Professor Claude Ghiglione.

1980's, when we described the preparation of new 5-nitroimidazoles bearing one or two tri- or tetra-substituted ethylenic double bonds at the 2 position by reacting original reductive alkylating agents with various aliphatic, cyclic or heterocyclic anions.[5] This work led us to synthesize the most active of all 5-nitroimidazole derivatives, the 1-methyl-3-(1-methyl-5-nitro-1*H*-imidazol-2-yl-methylene)pyrrolidin-2-one.[6]

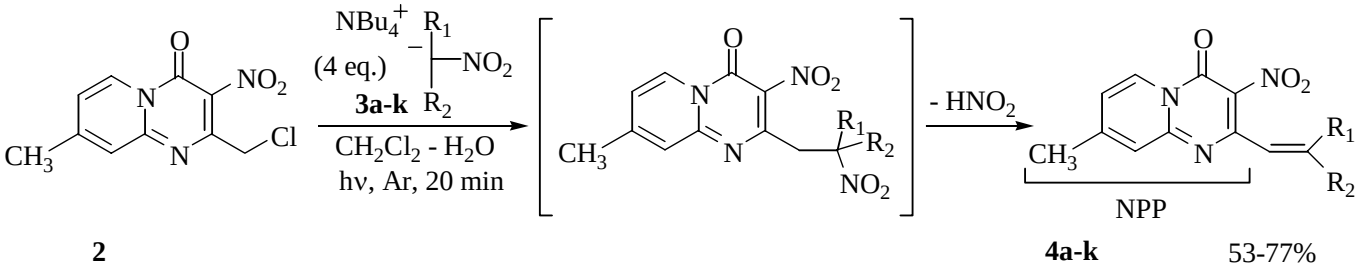
The interest of the pyrido[1,2-*a*]pyrimidine ring for medicinal chemistry led us to consider that electron transfer reactions might provide easy and versatile access to original 3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. By this strategy, we report here a new preparative method of potentially bioactive pyrimidinones. As suitable alkylating agent, we selected 2-chloromethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**2**). This chloride was easily obtained by cyclocondensation[7] of 2-amino-4-methylpyridine with ethyl 4-chloroacetoacetate and nitration with H_2SO_4/HNO_3 at 0 °C (Scheme 1).

Scheme 1

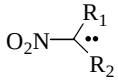
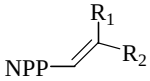
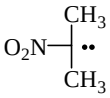
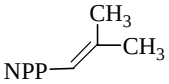
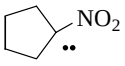
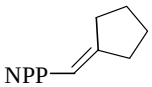
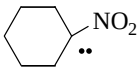
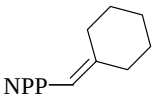
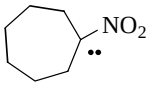
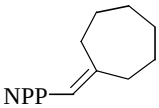
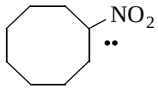
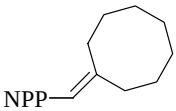
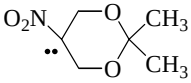
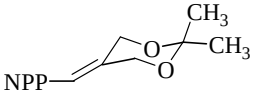
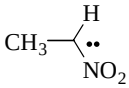
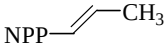
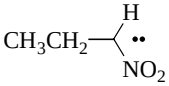
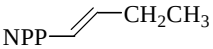
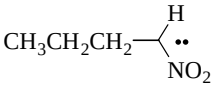
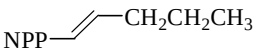
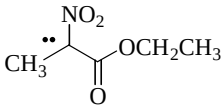
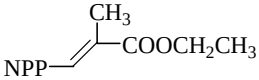
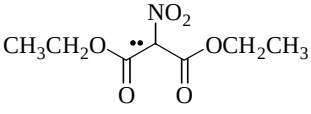
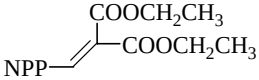


Derivative (**2**) was treated under nitrogen and photostimulation with various nitronate or malonate anions **(3a-k)**. By using 4 equivalents of anion during 20 min under phase-transfer conditions with 40% tetrabutylammonium hydroxide in water and dichloromethane,[8] we obtained the ethylenic derivatives (**4a-k)** in moderate to good yields (53 to 77%) as shown in Scheme 2 and indicated in the Table. This alkene was classically formed by electron transfer *C*-alkylation and base-promoted nitrous acid elimination from the *C*-alkylation product. The single electron transfer mechanism was confirmed in the reaction of **2** with 2-nitropropane anion (**3a**) by depression of reaction rate by addition of classical inhibitors[9] (*p*-dinitrobenzene as radical anion scavenger, 2,2,6,6-tetramethyl-1-piperidinyloxy or TEMPO as radical trap, bubbling dioxygen). When the ethylenic derivative was unsymmetrical, the stereochemistry of the double bond has been determinated by NMR (NOESY), and only the *E* isomer was isolated.

Scheme 2



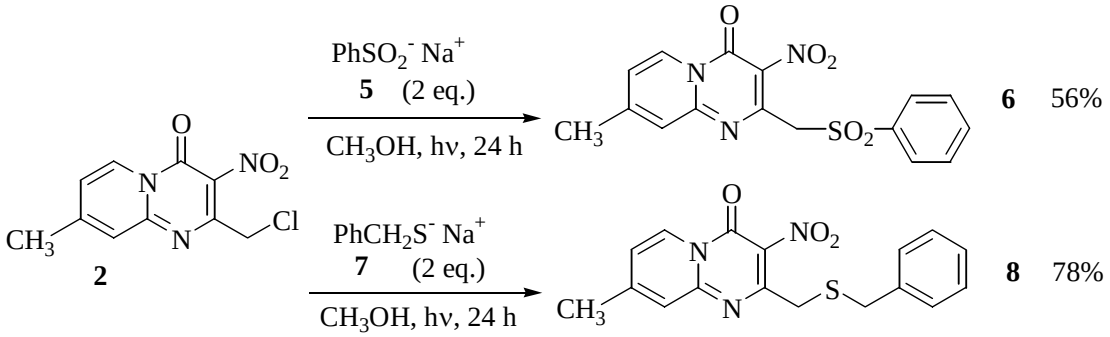
Table

Anion		Compound		**4** Yield (%)
3a		**4a**		77
3b		**4b**		70
3c		**4c**		66
3d		**4d**		57
3e		**4e**		54
3f		**4f**		53
3g		**4g**		77
3h		**4h**		61
3i		**4i**		54
3j		**4j**		68
3k		**4k**		65

As an understanding of the relationship between the nucleophile and the substrate in single electron transfer is useful in order to increase the selectivity and the yield of the reaction,[10] we have investigated the reactivity of **2** with other conventional nucleophiles as for example *S*-centred anions.[11] The reaction between the sodium salt of benzenesulfinic acid (**5**) or benzyl mercaptan (**7**) and **2** in degassed methanol gave the required products (**6**) and (**8**) respectively in 56 and 78% yields (Scheme 3). By addition of

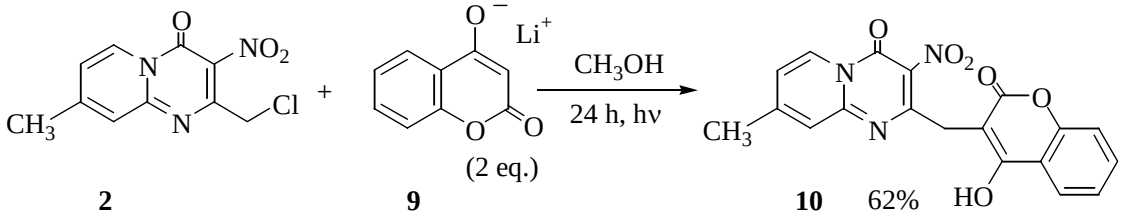
TEMPO in catalytic quantities or when the reaction was performed in the dark, the yields of **6** and **8** strongly decreased indicating that the single electron transfer mechanism is the most probable for the *S*-alkylation of chloride (**2**).

Scheme 3



Moreover, coumarins are a class of naturally occurring lactones, which display a wide range of biological activities.[12] Kornblum has studied alkylation of 2-carbethoxycoumaran-3-one in nitrobenzylic system *via* radical chain process.[13] Recently, the reaction of 4-hydroxycoumarins with a series of quinonic chlorides under photostimulation was shown to provide an efficient approach to 3-alkylated coumarin derivatives.[14] Radical reduction of **2** with lithium salt of 4-hydroxycoumarin (**9**) in degassed methanol under irradiation gave the *C*-alkylation product (**10**) in 62% yield as shown in Scheme 4.

Scheme 4



In conclusion, we have demonstrated here that this present methodology based on electron transfer reactions is a valuable and general method for the preparation of new potentially active pyrido[1,2-*a*]-pyrimidin-4-ones under mild operating conditions.

ACKNOWLEDGEMENTS

This work has been supported by the Centre National de la Recherche Scientifique and the Universities of Aix-Marseille. We express our thanks to Professor H. El-Kashef for stimulating discussions and M. Noailly for ^{1}H and ^{13}C NMR spectra recording. S. Djekou thanks the Ministry of National Education for a student research fellowship.

EXPERIMENTAL

Melting points were determined on Büchi B-540 and are uncorrected. Elemental analyses were performed by the Centre de Microanalyses of the University of Aix-Marseille 3 and of the INP-ENSCT (Toulouse, France). Both ^{1}H and ^{13}C NMR spectra were determined on a Bruker ARX 200 spectrometer. The ^{1}H chemical shifts are reported as parts per million downfield from tetramethylsilane (Me_4Si), and the ^{13}C chemical shifts were referenced to the solvent peak: $CDCl_3$ (76.9 ppm). Solvents were dried by conventional methods. The following adsorbent was used for column chromatography: silica gel 60 (Merck, particule size 0.063-0.200 mm, 70-230 mesh ASTM). TLC were performed on 5 cm x 10 cm aluminium plates coated with silica gel 60F-254 (Merck) in an appropriate solvent.

2-Chloromethyl-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (1)

A mixture of polyphosphoric acid (7.5 g), 2-amino-4-methylpyridine (1.35 g, 12.5 mmol) and ethyl 4-chloroacetoacetate (2.8 g, 17 mmol) was stirred at 110 °C for 5 h. After cooling, ice-cold solution of 10% sodium hydroxide (50 mL) was slowly added to adjust the pH to 7. The mixture was filtered and the precipitate was purified by chromatography on silica column eluting with dichloromethane-ether (6:4) and recrystallization from ethanol giving 1.9 g (73%) of yellow solid. **1**, mp 109 °C (mp 109-110 °C lit.,[7]), ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H); 4.46 (s, 2H); 6.62 (s, 1H); 6.98 (d, J = 7.3 Hz, 1H); 7.43 (br s, 1H); 8.98 (d, J = 7.3 Hz, 1H).

2-Chloromethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (2)

To a solution of 2-chloromethyl-8-methyl-*4H*-pyrido[1,2-*a*]pyrimidin-4-one (1 g, 4.8 mmol) in concentrated sulfuric acid (3 mL), fuming nitric acid (2 mL) was added dropwise at 0 °C. The reaction mixture was stirred at the same temperature for 1 h and poured into cold ice (50 mL). After filtration, the crude product was dissolved in dichloromethane (20 mL). The solvent was washed with saturated sodium bicarbonate solution (3 x 20 mL) and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, purification by chromatography on silica gel eluting with dichloromethane-ether (6:4) and recrystallization from ethanol gave 1.05 g (86%) of yellow solid. **2**, mp 170 °C, ^{1}H NMR ($CDCl_3$) δ 2.62 (s, 3H); 4.76 (s, 2H); 7.30 (d, J = 7.3 Hz, 1H); 7.67 (s, 1H); 9.08 (d, J = 7.3 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.89; 43.17; 121.02; 125.64; 128.38; 134.80; 150.43; 151.67; 153.79; 157.58. Anal. Calcd for $C_{10}H_8N_3O_3Cl$: C, 47.35; H, 3.18; N, 16.57. Found: C, 47.25; H, 3.14; N, 16.48.

The nitroalkanes were commercially available or prepared from the primary or secondary amines by oxidation with *m*-CPBA[15,16] in refluxed 1,2-dichloroethane for 3 h. 2,2-Dimethyl-5-nitro-1,3-dioxane[17] and ethyl 2-nitropropionate[18] were obtained as previously described. Diethyl nitromalonate was commercially available.

General procedure for the reactions of **2** with anions **(3a-k)**

Under nitrogen atmosphere, an aqueous solution of 40% tetrabutylammonium hydroxide in water (2.6 g, 4 mmol) reacted with nitroalkane (4 mmol) or 2,2-dimethyl-5-nitro-1,3-dioxane (0.64 g, 4 mmol) or ethyl 2-nitropropionate (0.58 g, 4 mmol) or diethyl nitromalonate (0.81 g, 4 mmol) for 1 h. A solution of **2** (0.25 g, 1 mmol) in dichloromethane (10 mL) was added and the mixture was stirred at rt during 20 min under nitrogen and irradiation with two 60 W tungsten lamps from a distance of 10 cm. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combinated organic layers were dried over magnesium sulfate and evaporated under reduced pressure. Purification by chromatography on silica column eluting with pentane-ether (8:2) (purification A) or dichloromethane-ethyl acetate (6:4) (purification B) and recrystallization from ethanol gave the required products **(4a-k)**.

8-Methyl-2-(2-methylpropenyl)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4a)

Yellow solid, 77% yield (purification A), mp 210 °C, ^{1}H NMR ($CDCl_3$) δ 2.07 (s, 3H); 2.23 (s, 3H); 2.56 (s, 3H); 6.31 (s, 1H); 7.12 (d, *J* = 7.3 Hz, 1H); 7.52 (s, 1H); 8.98 (d, *J* = 7.3 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.08; 21.74; 28.49; 117.58; 119.37; 125.00; 127.77; 133.83; 149.46; 151.51; 152.29; 155.81; 159.19. Anal. Calcd for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: C, 60.14; H, 5.05; N, 16.18.

2-Cyclopentylidenemethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4b)

Yellow solid, 70% yield (purification B), mp 209 °C, ^{1}H NMR ($CDCl_3$) δ 1.66-1.83 (m, 4H); 2.52-2.68 (m, 2H); 2.62 (s, 3H); 2.98-3.01 (m, 2H); 6.50 (s, 1H); 7.07 (d, *J* = 7.2 Hz, 1H); 7.67 (s, 1H); 8.96 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.60; 25.31; 26.84; 33.82; 37.64; 112.70; 118.93; 124.85; 127.58; 149.25; 151.06; 155.20; 167.71. Anal. Calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.23; H, 5.32; N, 14.71.

2-Cyclohexylidenemethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4c)

Yellow solid, 66% yield (purification B), mp 212 °C, ^{1}H NMR ($CDCl_3$) δ 1.56-1.63 (m, 6H); 2.31-2.34 (m, 2H); 2.54 (s, 3H); 2.75-2.78 (m, 2H); 6.25 (s, 1H); 7.09 (d, *J* = 7.3 Hz, 1H); 7.50 (s, 1H); 9.01 (d, *J* = 7.3 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.69; 26.26; 27.89; 28.64; 30.79; 38.73; 114.83; 119.33; 125.00; 127.73; 149.29; 151.43; 155.31; 158.74. Anal. Calcd for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.06; H, 5.69; N, 14.09.

2-Cycloheptylidenemethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4d)

Yellow solid, 57% yield (purification B), mp 239 °C, ^{1}H NMR ($CDCl_3$) δ 1.60-1.80 (m, 8H); 2.52-2.55 (m, 2H); 2.59 (s, 3H); 2.94-2.97 (m, 2H); 6.30 (s, 1H); 7.11 (d, *J* = 7.2 Hz, 1H); 7.48 (s, 1H); 8.99 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.63; 26.79; 28.17; 28.91; 29.52; 32.67; 40.09; 117.12; 119.18; 125.00; 127.63; 149.20; 151.22; 152.73; 155.72; 162.41. Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.16; H, 6.11; N,13.41. Found: C, 65.31; H, 6.09; N, 13.43.

2-Cyclooctylidenemethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4e)

Yellow solid, 54% yield (purification B), mp 223 °C, ^{1}H NMR ($CDCl_3$) δ 1.49-1.81 (m, 10H); 2.43-2.46 (m, 2H); 2.54 (s, 3H); 2.98-3.02 (m, 2H); 6.32 (s, 1H); 7.09 (d, *J* = 7.2 Hz, 1H); 7.45 (s, 1H); 8.98 (d, *J* = 7.2 Hz, 1H).^{13}C NMR ($CDCl_3$) δ 21.61; 25.57; 26.13; 26.60; 27.31; 27.65; 31.22; 39.80; 116.83; 119.08; 124.89; 127.57; 128.51; 149.16; 151.15; 151.56; 155.22; 164.86. Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.89; H, 6.44; N, 12.89.

2-[(2,2-Dimethyl-1,3-dioxan-5-ylidene)methyl]-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4f)

Yellow solid, 53% yield (purification A), mp 141 °C, ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3H); 1.39 (s, 3H); 2.54 (s, 3H); 4.07 (s, 2H); 4.38 (s, 2H); 5.52 (s, 1H); 7.31 (d, *J* = 6.9 Hz, 1H); 7.70 (s, 1H); 8.91 (d, *J* = 6.9 Hz, 1H).^{13}C NMR ($CDCl_3$) δ 21.78; 22.97; 23.49; 61.33; 63.53; 64.97; 86.74; 99.57; 119.84; 124.73; 127.95; 149.79; 152.46; 160.56. Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: C, 58.12; H, 5.16; N, 12.63.

8-Methyl-3-nitro-2-propenyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4g)

Yellow solid, 77% yield (purification B), mp 210 °C, *E* isomer, ^{1}H NMR ($CDCl_3$) δ 2.04 (q, *J* = 1.5 Hz, 3H); 2.53 (s, 3H); 6.66 (d, *J* = 13.4 Hz, 1H); 7.08 (d, *J* = 7.1 Hz, 1H); 7.40-7.57 (m, 1H); 7.66 (s, 1H); 8.95 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 20.95; 21.64; 119.02; 121.25; 124.80; 127.57; 127.72; 148.86; 149.52; 151.47; 151.71; 153.54. Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.13. Found: C, 58.69; H, 4.57; N, 17.15.

2-But-1-enyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4h)

Yellow solid, 61% yield (purification B), mp 187 °C, *E* isomer, ^{1}H NMR ($CDCl_3$) δ 1.13 (t, *J* = 7.4 Hz, 3H); 2.28-2.44 (m, 2H); 2.53 (s, 3H); 6.62 (d, *J* = 15 Hz, 1H); 7.08 (d, *J* = 7.1 Hz, 1H); 7.36-7.50 (dd, *J* = 15 Hz and 6.6 Hz, 1H); 7.47 (s, 1H); 8.95 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 12.49; 21.63; 26.29; 119.01; 121.26; 124.78; 127.56; 127.70; 148.89; 149.51; 151.44; 151.70; 153.54. Anal. Calcd for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: C, 60.13; H, 5.01; N, 16.29.

8-Methyl-3-nitro-2-pent-1-enyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4i)

Yellow solid, 54% yield (purification B), mp 162 °C, *E* isomer, ^{1}H NMR ($CDCl_3$) δ 1.01 (t, *J* = 7.3 Hz, 3H); 1.47-1.62 (m, 2H); 2.26-2.37 (m, 2H); 2.53 (s, 3H); 6.64 (d, *J* = 15 Hz, 1H), 7.08 (d, *J* = 7.1 Hz, 1H), 7.32-7.43 (dd, *J* = 15 Hz and 6.5 Hz, 1H), 7.48 (s, 1H), 9.03 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 13.79; 21.64; 22.34; 26.29; 119.01; 121.26; 124.78; 127.56; 127.70; 148.89; 149.51; 151.44; 151.70; 153.54. Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.61; H, 5.58; N, 15.30.

Ethyl 2-methyl-3-(8-methyl-3-nitro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-2-yl)acrylate (4j)

Yellow solid, 68% yield (purification A), mp 145 °C, *E* isomer, ^{1}H NMR ($CDCl_3$) δ 1.35 (t, *J* = 7.1 Hz, 3H); 2.25 (s, 3H); 2.60 (s, 3H); 4.28 (q, *J* = 7.1 Hz, 2H); 7.18 (d, *J* = 7.2 Hz, 1H); 7.58 (s, 1H); 7.61 (s,

1H); 9.09 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 14.14; 14.75; 21.77; 61.50; 120.44; 125.43; 128.06; 129.86; 138.29; 141.26; 149.74; 151.10; 152.95; 155.54; 167.05. Anal. Calcd for $C_{15}H_{15}N_3O_5$: C, 56.78; H, 4.76; N, 13.24. Found: C, 56.81; H, 4.75; N, 13.20.

Diethyl 2-[(8-methyl-3-nitro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-2-yl)methylene]malonate (4k)

Yellow solid, 65% yield (purification A), mp 152 °C, ^{1}H NMR ($CDCl_3$) δ 1.31 (t, *J* = 7.1 Hz, 3H); 1.35 (t, *J* = 6.9 Hz, 3H); 2.59 (s, 3H); 4.34 (q, *J* = 7.1 Hz, 2H); 4.37 (q, *J* = 6.9 Hz, 2H); 7.21 (d, *J* = 7.2 Hz, 1H); 7.46 (br s, 1H); 7.79 (s, 1H); 9.08 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 14.02; 14.09; 21.86; 61.50; 62.40; 120.65; 125.30; 128.32; 132.89; 134.77; 142.01; 149.45; 151.10; 152.59; 153.35; 162.77; 164.93. Anal. Calcd for $C_{17}H_{17}N_3O_7$: C, 54.40; H, 4.57; N, 11.20. Found: C, 54.21; H, 4.63; N, 11.28.

Sodium salt of benzenesulfinic acid was commercially available.

Preparation of the sodium salt of benzyl mercaptan (**7**) and the lithium salt of 4-hydroxycoumarine (**9**)

A sodium or lithium methoxide was prepared by careful addition of sodium (0.58 g, 0.025 at.g) or lithium (0.17 g, 0.025 at.g) to methanol (15 mL). After the solution had become clear, benzyl mercaptan (3.10 g, 0.025 mol) or 4-hydroxycoumarine (4.05 g, 0.025 mol) was added, the solution was stirred at rt for 2 h and concentrated under vacuum. When the solution became viscous, about 300 mL of ether was added to cause precipitation. The sodium salt (**7**) or lithium salt (**9**) was filtered, washed by ether and kept under oil-pump vacuum for 24 h.

General procedure for the reaction of **2** with anions (**5**) or (**7**) or (**9**)

To a solution of **2** (0.25 g, 1 mmol) in dry methanol (5 mL), sodium salt of benzenesulfinic acid (0.32 g, 2 mmol) or sodium salt of benzyl mercaptan (0.29 g, 2 mmol) or lithium salt of 4-hydroxycoumarine (0.33 g, 2 mmol) was added under dry nitrogen. The reaction mixture was then irradiated with fluorescent lamps. After stirring at rt for 24 h, methanol was evaporated under reduced pressure. Purification by chromatography on silica column eluting with pentane-ether (8:2) and recrystallization from ethanol gave the required products.

2-Benzenesulfonylmethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6)

Yellow solid, 56% yield, mp 177 °C, ^{1}H NMR ($CDCl_3$) δ 2.59 (s, 3H); 4.93 (s, 2H); 7.28 (d, *J* = 7.3 Hz, 1H); 7.49-7.89 (m, 5H); 7.87 (s, 1H); 9.07 (d, *J* = 7.3 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.86; 58.13; 121.07; 125.46; 128.30; 129.34; 134.29; 138.93; 149.60; 150.50; 150.92; 153.91. Anal. Calcd for $C_{16}H_{13}N_3O_5S$: C, 53.48; H, 3.65; N, 11.69. Found: C, 53.39; H, 3.72; N 11.70.

2-Benzylsulfanylmethyl-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (8)

Yellow solid, 78% yield, mp 111 °C, ^{1}H NMR ($CDCl_3$) δ 2.55 (s, 3H); 3.58 (s, 2H); 5.66 (s, 2H); 7.33 (d, *J* = 7.25 Hz, 1H); 7.42 (s, 1H); 7.67-7.70 (m, 5H); 9.01 (d, *J* = 7.25 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.64; 29.68; 43.22; 127.40; 128.47; 129.28; 129.39; 130.19; 133.80; 137.32; 138.90; 151.49; 153.11; 155.14; 172.28. Anal. Calcd for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31. Found: C, 59.65; H, 4.39; N, 12.27.

2-[(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)methyl]-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (10)

Yellow solid, 62% yield, mp 214 °C, ^{1}H NMR ($CDCl_3$) δ 2.54 (s, 3H); 5.48 (s, 2H); 5.61 (s, 1H); 7.18-7.28 (m, 4H); 7.48 (br s, 1H); 7.75 (d, *J* = 9.7 Hz, 1H); 9.01 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.86; 66.22; 91.62; 115.21; 116.71; 120.85; 121.18; 123.19; 123.96; 124.28; 125.83; 128.52; 132.74; 150.10; 153.25; 154.12; 156.30; 162.74; 165.11. Anal. Calcd for $C_{19}H_{13}N_3O_6$: C, 60.16; H, 3.45; N, 11.08. Found: C, 60.06; H, 3.57; N, 11.19.

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